

Switch to Mania After Slow rTMS of the Right Prefrontal Cortex

Sir: Recent evidence indicates that slow repetitive transcranial magnetic Stimulation (rTMS) of the right dorsolateral prefrontal cortex (DLPFC) exerts antidepressant effects.¹ Here, we report on 2 patients suffering from a therapy-resistant major depressive episode who had given their written informed consent to participate in a controlled rTMS trial. Both patients underwent 1-Hz rTMS of the right DLPFC and switched from depression to a manic state.

Case 1. A 79-year-old woman, suffering from a recurrent major depressive disorder (DSM-IV) since menopause, underwent 3 adequate antidepressant trials during the current severe depressive episode without clinical improvement. The last medication (20 mg of tranylcypromine, 6 mg of haloperidol, and 0.5 mg of lorazepam) was kept constant for 3 weeks prior to rTMS. The patient underwent 10 rTMS sessions within 2 weeks at the following stimulation parameters: 1 Hz, 110% of motor threshold intensity, 1200 stimuli/day. Scores on the Hamilton Rating Scale for Depression (HAM-D) declined slightly during rTMS (day 0, HAM-D score = 34; day 14, HAM-D score = 29). Lorazepam was discontinued and haloperidol slightly reduced after the last rTMS session. Three days after the last session, the patient developed a severe manic state for 2 days. She became hyperactive, developed a strong appetite, took up smoking, and requested a guitar (Young Mania Rating Scale [YMRS] score = 32). The patient then switched back to a depressive mood and recovered 5 weeks later during valproate and sertraline treatment.

Case 2. A 46-year-old businessman who had been suffering from a pharmacotherapy-resistant severe bipolar I depressive episode (DSM-IV) for 3 years was hospitalized for rTMS and successive ECT. At admission, sertraline, reboxetine, and quetiapine were continued but lamotrigine was stopped in preparation for ECT. Reboxetine was also discontinued due to the patient's severe agitation. Two weeks after admission, the patient underwent 15 rTMS sessions within 3 weeks at the following stimulation parameters: 1 Hz, 110% of motor threshold intensity, 1200 stimuli/day. Depressive symptoms declined (day 0, HAM-D score = 30; day 21, HAM-D score = 16). Mood improvement continued after rTMS, and the patient became manic 7 days after the last session. He dressed fancily, invested thousands of dollars, began to smoke after long abstinence, and became hypersexual (YMRS score = 23). Lamotrigine was started; sertraline was tapered off. After 2 weeks of treatment with quetiapine and lamotrigine without clinical improvement, he received a further 15 sessions of 10-Hz rTMS of the right DLPFC as a putative antimanic treatment.^{2,3} Manic symptoms increased during rTMS, but he recovered with risperidone and valproate treatment.

Switches to mania are frequently seen in bipolar patients during antidepressant pharmacotherapy.⁴ Similarly, 3 cases have been recently reported in patients suffering from a bipolar I or II disorder after fast rTMS of the left DLPFC.^{5,6} Our cases show that manic switches can also occur subsequent to slow (1 Hz) rTMS of the right DLPFC and even in hitherto unipolar depressive patients. However, disorientation effects, which have been previously reported for lorazepam⁷ and anticonvulsants,⁸ may have contributed to the switches.

In both cases, depressive symptoms remained therapy-resistant during antidepressant pharmacotherapy prior to rTMS, further supporting the possibility of a causal relationship between rTMS and the subsequent switches.

The present cases underline the importance of intensive follow-up after rTMS in patients at risk for bipolar switches. Furthermore the risk of switching should be explained to depressed patients participating in therapeutic rTMS trials.

This work was supported by the German Ministry for Education and Research within the promotional emphasis "German Research Network on Depression" (subproject 6.5, Dr. Padberg).

REFERENCES

1. Klein E, Kreinin I, Chistyakov A, et al. Therapeutic efficacy of right prefrontal slow repetitive transcranial magnetic stimulation in major depression: a double-blind controlled study. *Arch Gen Psychiatry* 1999; 56: 315-320
2. Grisaru N, Chudakov B, Yaroslavsky Y, et al. Transcranial magnetic stimulation in mania: a controlled study. *Am J Psychiatry* 1998; 155: 1608-1610
3. Erfurth A, Michael N, Mostert C, et al. Euphoric mania and rapid transcranial magnetic Stimulation. *Am J Psychiatry* 2000; 157: 835-836
4. Himmelhoch JM, Thase ME, Mallinger AG, et al. Tranylcypromine versus imipramine in anergic bipolar depression. *Am J Psychiatry* 1991; 148: 910-916
5. Dolberg OT, Schreiber S, Grunhaus L. Transcranial magnetic stimulation induced switch into mania: a report of two cases. *Biol Psychiatry* 2001; 49: 468-470
6. Garcia-Toro M. Acute manic symptomatology during repetitive transcranial magnetic stimulation in a patient with bipolar depression [letter]. *Br J Psychiatry* 1999; 175: 491
7. Turkington D, Gill P. Mania induced by lorazepam withdrawal: a report of two cases. *J Affect Disord* 1989; 17: 93-95
8. Scull DA, Trimble MR. Mania precipitated by carbamazepine withdrawal [letter]. *Br J Psychiatry* 1995; 167: 698

Robin Ella, M.D.
Peter Zwanzger, M.D.
Robert Stampfer, M.D.
Ulrich W. Preuss, M.D.
Florian Müller-Siecheneder, M.D.
Hans-Jürgen Möller, M.D.
Frank Padberg, M.D.
Ludwig-Maximilian University
Munich, Germany

Exacerbation of Idiopathic Priapism With Risperidone-Citalopram Combination

Sir: Polypharmacy is an increasingly recognized risk factor for unintended medication side effects and adverse events. Recently, a case of priapism attributed to combined treatment with risperidone, olanzapine, and fluvoxamine was described.¹ I report a case of worsening idiopathic priapism while a patient was treated with the antipsychotic risperidone and the selective serotonin reuptake inhibitor citalopram.

Case report. Mr. A, a 29-year-old man from the Congo with never-treated paranoid schizophrenia (DSM-IV), was committed for 6 months to an inpatient unit. He had an excellent response to monotherapy with 4 mg of risperidone daily. A few months into treatment, he developed a severe postpsychotic major depressive episode (DSM-IV) with somatic delusions for which citalopram, 40 mg p.o. q.d., was added to his maintenance risperidone dose of 3 mg daily. About 4 weeks into treatment with the risperidone-citalopram combination, he