

### Transient Complex Visual Hallucinations With Venlafaxine Treatment: A Case Report

**Sir:** Antidepressants have been noted to cause hallucinations, often with drug overdose, but also in rare instances as a side effect at therapeutic dose.<sup>1</sup> Bupropion, tricyclics, and selective serotonin reuptake inhibitors (SSRIs) have most often been cited as the causative agents.<sup>1</sup> We present a case of transient complex visual hallucinations following the initiation of venlafaxine for major depressive disorder.

**Case report.** Mr. A was a 44-year-old man recovering from alcohol dependence in an outpatient partial hospitalization program. He had been recently hospitalized for delirium tremens and was discharged 3 days before admission to our outpatient program in December 2007. He began venlafaxine treatment, 75 mg daily, for depression 2 weeks after his last drink. Before initiation of treatment, he had had no auditory or visual hallucinations for 10 days and no history of psychotic disorders or manic symptoms. He was diagnosed according to DSM-IV-TR with alcohol dependence and recurrent major depressive disorder without psychosis.

Mr. A had been 3 weeks' sober when, after 1 week of venlafaxine treatment, he reported having visual hallucinations during daytime group sessions: seeing an acetylene torch in his hand and trying to strike it against his desk to light it as well as nodding his head to drop a welding shield over his face, as he did when he worked as a welder. He had insight that these were hallucinations. He had no delusions or hallucinations in other modalities, no manic symptoms, and no altered mental status. The only other side effect noted was increased vividness to his dreams. The only other medication changes were the addition of lactulose for mildly elevated ammonia, 41  $\mu\text{mol/L}$  at the onset of hallucinations.

After 1 week, his hallucinations resolved, and he had no repeat episodes. The venlafaxine dose was maintained throughout his treatment. He completed the outpatient program and was discharged without further incidents 3 weeks later, and at 2 monthly follow-up appointments he reported no additional hallucinations.

Antidepressants have been cited as inducing hallucinations in rare cases. There have been 2 reports of venlafaxine-induced hallucinations, in an adolescent patient and an adult patient.<sup>2,3</sup> Given that Mr. A's dose was low (75 mg daily), the assumed mechanism of action for hallucinosis is serotonergic, not norepinephrinergic. Some studies have suggested that SSRIs may induce psychotic symptoms by 5-HT<sub>2</sub>- and 5-HT<sub>3</sub>-mediated dopamine release in the ventral striatum.<sup>4</sup> Venlafaxine may have produced visual hallucinations via dopamine release in the mesolimbic pathway by stimulation of 5-HT<sub>2</sub> and 5-HT<sub>3</sub> receptors.

A possible interaction could have been reactivation of alcoholic hallucinosis with venlafaxine, which was reported with sertraline in 1 case by Hermann et al.<sup>5</sup> However, the causative mechanism in that case was felt to be due to increased dopamine availability. Sertraline shows the greatest amount of dopamine reuptake inhibition of all SSRIs, while venlafaxine shows no inhibition of the dopamine reuptake transporter.

Lastly, our patient's ammonia was mildly elevated, and treatment could have exacerbated a subclinical hepatic

encephalopathy, although no altered mental status or other signs of delirium were observed during his partial hospitalization.

*The authors report no financial or other relationships relevant to the subject of this letter.*

#### REFERENCES

1. Cancelli I, Marcon G, Balestrieri M. Factors associated with complex visual hallucinations during antidepressant treatment. *Hum Psychopharmacol* 2004;19(8):577-584
2. Emslie GJ, Yeung PP, Kunz NR. Long-term, open-label venlafaxine extended-release treatment in children and adolescents with major depressive disorder. *CNS Spectr* 2007;12(3):223-233
3. Anghelescu I, Klawe C, Himmerich H, et al. Topiramate in venlafaxine-induced visual hallucinations in an obese patient with a posterior cerebral artery infarction [letter]. *J Clin Psychopharmacol* 2001;21(4):462-464
4. Schuld A, Archelos JJ, Friess E. Visual hallucinations and psychotic symptoms during treatment with selective serotonin reuptake inhibitors: is the sigma receptor involved? [letter] *J Clin Psychopharmacol* 2000;20(5):579-580
5. Hermann D, Heinz A, Croissant B, et al. Serotonin reuptake inhibitor provoked recurrence of alcohol hallucinosis—remission with additive amisulpride medication: a case report [letter]. *Pharmacopsychiatry* 2004;37(2):90-92

**Adam C. Tripp, M.D., Ph.D.**

Western Psychiatric Institute & Clinic  
University of Pittsburgh Medical Center

**Scott A. Golden, M.D.**

Behavioral Health Division  
Veterans Hospital at Highland Drive  
Pittsburgh, Pennsylvania

© Copyright 2009 Physicians Postgraduate Press, Inc.

### Repetitive Transcranial Magnetic Stimulation for Premenstrual Dysphoric Disorder: A Case Report

**Sir:** Tan et al.<sup>1</sup> describe an antidepressant effect of repetitive transcranial magnetic stimulation (rTMS) in a pregnant woman with recurrent major depressive disorder. The association of estrogen and depressive disorder is well known.

Premenstrual syndrome (PMS) occurs in women of childbearing age in the second half of the menstruation cycle and consists of emotional, behavioral, and physical symptoms. When symptoms are so severe that daily activities are disrupted, a diagnosis of premenstrual dysphoric disorder (PMDD) may be given.

Possible causes are extraordinary sensitivity to the normal fluctuations of hormone production during the menstrual cycle and pathological reactions to the changes in the neurotransmitter serotonin. For the last reason, antidepressants such as selective serotonin reuptake inhibitors (SSRIs) may be helpful.

To my knowledge, no studies have systematically examined the treatment of PMDD with rTMS, which has been proven effective for treating depressions, although only short-term effects have been reported.<sup>2</sup> In a single case observation, we saw some benefit also in treating a patient with attention-deficit/hyperactivity disorder.<sup>3</sup>

## LETTERS TO THE EDITOR

**Case report.** In 2006, Ms. A, the 41-year-old female patient of this observation, had DSM-IV–defined PMDD and was evaluated 1 week before menstruation in the active arm of the rTMS trial and 10 days before menstruation in the placebo (sham) arm of the trial.<sup>3</sup> There were no comorbidities except a slightly diminished concentration span. The patient received no additional medication during this period.

Low frequency rTMS (1 Hz, 1200 stimulations per day, lasting 1 hour, for 5 days) was applied on the impending scalp motor area. Symptomatology was evaluated by the Hamilton Rating Scale for Depression<sup>4</sup> (HAM-D; 21 items to be rated on a 2–4 step Likert scale, maximum score of 66), before and after the 5-day treatment with rTMS.

Ms. A's initial HAM-D score was 41 (active treatment) and 38 (placebo); after the active treatment, the patient's score improved to 29, and after placebo treatment 4 months later (the coil was applied in the same way as 4 months before, but not activated), to 36. The effect lasted until the end of the next menstruation. In the next cycle, no improvement could be observed. Electroencephalogram and laboratory parameters (red blood cell count, white blood cell count, and liver transaminase) were found to be within the normal range before and after the treatment with active and placebo rTMS. No adverse side effects could be observed.

We assume that rTMS might also show some benefit in the treatment of PMS, which has been described to last for a short time (3 days) and to respond with antidepressants. Also, rTMS

seems to have a slight effect during menstruation. If a patient responds well, rTMS should be repeated at each menstruation cycle. Furthermore, rTMS could be an effective add-on therapy to reduce the dosage of antidepressants or hormones. Further controlled studies are urgently warranted.

*Dr. Niederhofer reports no financial affiliations or other relationships relevant to the subject of this letter.*

### REFERENCES

1. Tan O, Tarhan N, Coban A, et al. Antidepressant effect of 58 sessions of rTMS in a pregnant woman with recurrent major depressive disorder: a case report [letter]. *Prim Care Companion J Clin Psychiatry* 2008;10(1):69–71
2. Fregni F, Marcolin MA, Myczkowski M, et al. Predictors of antidepressant response in clinical trials of transcranial magnetic stimulation. *Int J Neuropsychopharmacol* 2006;9(6):641–654
3. Niederhofer H. Effectiveness of the repetitive transcranial magnetic stimulation (rTMS) of 1 Hz for attention-deficit/hyperactivity disorder (ADHD). *Psychiatr Danub* 2008;20:91–92
4. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry* 1960;23:56–62

**Helmut Niederhofer, M.D., Ph.D., M.A.S.**  
Department of Pediatrics and Child Psychiatry  
General Hospital of Bolzano  
Bolzano, Italy

© Copyright 2009 Physicians Postgraduate Press, Inc.