Safety and Feasibility of Repetitive Transcranial Magnetic Stimulation in the Treatment of Anxious Depression in Pregnancy: A Case Report

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Background: The proper treatment of mood disorders occurring during pregnancy is a major therapeutic problem since no antidepressant medications have been established as safe for the developing fetus. Several double-blind placebo-controlled studies have explored the efficacy of repetitive transcranial magnetic stimulation (rTMS) in depression.

Case: We report the case of a 36-year-old woman in her second trimester of pregnancy, whose depression (DSM-IV) and anxiety were successfully treated with rTMS. Further studies of rTMS in depressed pregnant women appear warranted.

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The proper treatment of mood disorders occurring during pregnancy is a major therapeutic problem, since no antidepressant medications have been established as safe for the developing fetus.[1] However, left untreated, depression itself is risky to both mother and baby, and that risk must be weighed against the risk of treatment.[2,3] In severe cases, electroconvulsive treatment (ECT) is often believed to be the safest alternative.[4]

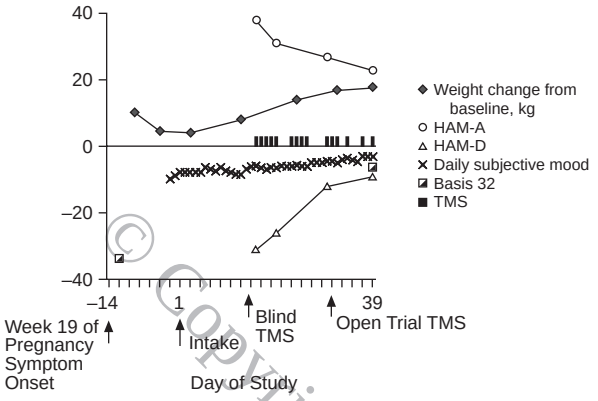
Repetitive transcranial magnetic stimulation (rTMS) is a relatively new, noninvasive technique for probing brain function.[5] TMS involves placing an electromagnet on the scalp and applying pulsed magnetic stimulation, which passes relatively unimpeded through the soft tissues of the head. Oscillations in the magnetic field induce an electrical current flow in cortical tissue, resulting in neuronal depolarization, which moves to deeper subcortical structures by transsynaptic transmission. While TMS single pulses cause neurons to fire and are thus excitatory, rapid trains of stimulation, rTMS, cause almost constant firing, prolonging the effective refractory period of the neurons and creating a temporary inhibitory functional lesion that disrupts behavior.[6] rTMS has been used in a variety of brain mapping techniques and has shown promise as a potential treatment in Parkinson's disease, cortical epilepsy, and depression.[7]

To date, several double-blind placebo-controlled studies have explored the efficacy of rTMS in depression with a wide range of clinical presentations (moderate depression to psychotic depression)[8–10] and different age groups. However, to our knowledge, the use of rTMS to treat depression during pregnancy has not been explored. Here, we report the case of a 36-year-old woman in her second trimester of pregnancy, treated with rTMS as part of an ongoing placebo-controlled blind study for evaluation of efficacy and optimal frequency of rTMS-treatment in depression.

CASE REPORT

Ms. A, a 36-year-old married professional, became pregnant with her first child after 2 years of no contraceptive use. She was monitored closely by her obstetrician and was judged to be progressing normally as indicated by her first ultrasound, amniocentesis, and regular obstetric examinations. At 17 weeks, 1 week into recovering from bronchitis, she experienced an acute panic attack with agoraphobia while on a plane on a routine business trip. Her symptoms rapidly worsened over the course of several days to include depressed and anxious mood, severe restlessness and insomnia, constant worries about the health of her baby, obsessive ruminations concerning her lack of appetite, and the apprehension of being hospitalized and tube-fed. She had lost 6 lb (2.8 kg) from the onset of pregnancy by the time she presented to our research

Figure 1. Low-Frequency Daily Left Prefrontal Repetitive Transcranial Magnetic Stimulation (TMS) in a Depressed Anxious Pregnant Woman[a]



[a]Abbreviations: Basis 32 = Behavior and Symptom Identification Scale,[18] HAM-A = Hamilton Rating Scale for Anxiety, HAM-D = Hamilton Rating Scale for Depression.

setting at 19-weeks of gestation. At that time, she was unable to sit still, was constantly pacing and clenching her fists, had difficulty maintaining focus, and could attend to a conversation only with effort. She had taken some time off from her job as a computer consultant. Her personal history was void of any psychiatric precedents or major developmental epigenetic causes. Her family history included a father with posttraumatic stress disorder from active military duty currently taking paroxetine, and 1 paternal aunt who had been treated for depression.

After the initial evaluation, an extended medical and obstetrical workup ruled out any medical cause to her symptoms (the workup included a cell blood count, a chemistry panel including liver function tests, thyroid functions, and HIV screening). A meeting was held with the patient and her family to extensively discuss her treatment options and the risks from enrolling in our study. She refused antidepressant medications because of their unknown effect on her fetus and decided to try active counseling. With minimal improvement after 2 weeks of supportive counseling, at the rate of once per week, she decided to enroll in our rTMS study and signed an informed consent form.

She was reevaluated for research diagnostic purposes with the Schedule for Affective Disorders and Schizophrenia (SADS)[11] and was rated on the Hamilton Rating Scale for Depression (HAM-D),[12] Hamilton Rating Scale for Anxiety (HAM-A),[13] Mini-Mental State Examination (MMSE),[14] Beck Depression Inventory,[15] and Clinical Global Impressions Scale[16] (Figure 1). She met the DSM-IV criteria for major depressive disorder, but not for obsessive-compulsive disorder. She maintained her own daily subjective mood chart and had double-blind objective mood ratings. She underwent a baseline 1.5 Tesla structural and perfusion functional magnetic resonance image (fMRI) scan to rule out organic causes for a risk of seizure and to obtain a baseline functional brain activity scan.

Treatment Course

At week 22 of pregnancy, she was randomly assigned to receive active low-frequency stimulation (5 Hz, 5 seconds on, 25 seconds off, over 20 minutes) at 100% of motor threshold, and was stimulated once a day for 5 days over a 9-day period. Her motor threshold was checked daily and averaged 48% at maximum machine output (Cadwell High Speed Stimulator, figure 8 water-cooled coil, Kennewick, Wash.). There was no change in her blood pressure, O_2 saturation, or heart rate during any of the procedures or over the course of the 2-week treatment. She was then tapered off rTMS in an open trial over the course of 5 sessions (total of 14 days of treatment during 3 weeks).

Outcome

Ms. A tolerated the treatment well. She initially had apprehension of the stimulation and the noise, but that apprehension subsided. She repeatedly experienced a "calming effect" around minute 12 of the stimulation session. She described herself as "relaxed and tired." On day 6 of stimulation, this relaxed effect would occur around minute 3 of the session. She denied impaired cognition, headaches, and discomfort during the sessions. On her second day only, she experienced tension in her abdominal muscles at the pelvic line, which was attributable to her tension and anxiety and which never recurred. Upon later questioning, she never endorsed this symptom again.

Ms. A's improvement was noticeable on several levels and was documented with double-blind ratings (Figure 1).

Clinically, on her first weekend of treatment she went shopping with a friend and attended an engagement party. After 9 days of treatment, she attended a job meeting out of town and has not experienced any recurrence of her ruminations or uncertainties. She was able to be tapered off her nightly dose of acetaminophen and diphenhydramine (Tylenol P.M.). Her affect became bright, her conversation more elaborate, and she was minimally somatic. She appeared relaxed and was actively engaged in preparations for her upcoming business meeting. Periodic follow-up revealed that she remained in remission, and she delivered a healthy 7.5 lb (3.4 kg) baby boy at term.

DISCUSSION

This case illustrates a marked improvement of an episode of depression combined with anxious features during pregnancy that was achieved through a course of double-blind, low-frequency, left prefrontal rTMS. The patient's positive response could be attributable to several

other causes, such as spontaneous remission, behavioral modifications, the reassurance of treatment, or frequent visits with treating physicians and multiple ratings. Although these could be contributory or even causal, we reason that they played only a moderate role (if any) in her improvement. For example, her symptoms were severe and did not improve when she was given frequent counseling.

The mechanisms through which rTMS affects brain metabolism, and ultimately behavioral manifestations and clinical outcomes, are still unknown. This case is the first using rTMS as an alternative treatment in mood disorders and pregnancy. It demonstrates a positive outcome along with a safe profile. rTMS has a minimal risk of seizure in controlled settings and under well-guided stimulation parameters,[17] and most importantly, rTMS involves no fetal exposure to anesthetics as with ECT or psychotropic medications. Further controlled studies appear warranted to evaluate this new treatment modality in depression and pregnancy.

Drug name: paroxetine (Paxil).

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