Despite the role of anxiety in these previous studies, in our analysis, we found that agitation, less retardation, less depressed mood, less somatic symptoms, and more weight loss seem to characterize the caregivers of symptomatic versus asymptomatic children. When comparing only caregivers of symptomatic children, those caring for children with impact presented higher levels of anxiety, which is in line with the existing literature. Greater knowledge of mechanisms underlying caregiver-offspring interactions is needed to improve treatment strategies.

Camila T. Matsuzaka,[1] Milton L. Wainberg,[2,3] Andrea Norcini Pala,[3,4] Marcelo F. Mello[1]
[1]*Departamento de Psiquiatria, Universidade Federal de São Paulo (UNIFESP), São Paulo, SP, Brazil.* [2]*Division of Epidemiology, New York State Psychiatric Institute, New York, NY, USA.* [3]*Department of Psychiatry, Columbia University College of Physicians and Surgeons, New York, NY, USA.* [4]*HIV Center for Clinical and Behavioral Studies, New York State Psychiatric Institute, New York, NY, USA.*

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Repetitive transcranial magnetic stimulation for the treatment of major depression during pregnancy

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The prevalence of mental disorders is high among pregnant women.[1] Major depression during pregnancy is a risk factor for negative outcomes for both mother and child.[2] Psychotherapy and pharmacotherapy are well-established conventional treatments for depression. However, some cases fail to respond, and the safety of some psychopharmaceuticals during pregnancy is unclear. Within this context, certain neuromodulation techniques, including repetitive transcranial magnetic stimulation (rTMS), have been studied in pregnant women with depression.

A review of the recent literature[3] suggested that rTMS is an effective alternative for the treatment of depression in pregnant women, and there have been no reports of malformations or other relevant negative fetal outcomes.[4] However, use of the rTMS technique in pregnant women has only been evaluated in one open study[5] and a few case reports; there have been no randomized clinical trials evaluating its use in this setting. Here, we report the cases of four nulliparous pregnant women (one with a twin pregnancy) diagnosed with major depressive disorder and treated with rTMS.

Sociodemographic and clinical features are summarized in Table 1. In three patients, rTMS was applied to the left dorsolateral prefrontal cortex (DLPFC) at 3,000 pulses/session (120% of the motor threshold; frequency 10 Hz; figure-eight coil). In the remaining patient, rTMS was applied to the right DLPFC at 1,800 pulses/session (120% of the motor threshold; frequency 1 Hz; figure-eight coil). To evaluate symptoms of depression and anxiety, the 21-item Hamilton Depression Rating Scale (HDRS-21), the 14-item Hamilton Anxiety Rating Scale (HARS-14), and the Clinical Global Impression-Severity (CGI-S) scale were applied before and after rTMS. Three of the patients were medicated, two with sertraline and one with fluoxetine, and the prescribed dosages were maintained throughout rTMS treatment.

According to the HDRS-21 and HARS-14, all patients presented a response, with a 65% mean reduction in depressive and anxiety symptoms. CGI-S scores also showed a 66% reduction in depressive symptoms. All patients tolerated the treatment, although all but one reported some side effects. None of the patients had complications at delivery. All infants had 5-minute Apgar scores of 9, except for the twins born to patient 2, who were preterm (36 weeks) and had Apgar scores of 6 and 8.

Our results are in agreement with existing experience regarding the responses obtained with rTMS in pregnant women with depression. Our choice of the prefrontal cortex as the rTMS target was based on previous reports.[5,6] The frequency of stimulation varies according to the side of application. Studies of rTMS in pregnant women with depression have employed 10-25 Hz and 1 Hz in the left and right DLPFC, respectively, quite similar to the frequencies used in the general population of adults with depression.[2] Despite these promising findings, there is a need for controlled, double-blind studies involving larger samples, with well-designed rTMS parameters, and even for prospective studies (following pregnant women and their offspring) to assess the long-term safety of rTMS in children exposed *in utero*.

Ygor Arzeno Ferrão,[1] Renata de Melo Felipe da Silva[2]
[1]*Departamento de Psiquiatria, Universidade Federal de Ciências da Saúde de Porto Alegre, Porto Alegre, RS, Brazil.* [2]*Faculdade de Medicina, Universidade de São Paulo (FMUSP), São Paulo, SP, Brazil.*

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Table 1 Sociodemographic and clinical features of four pregnant women who received rTMS for major depression, and 5-minute Apgar scores for their children

Variable	Patient 1	Patient 2	Patient 3	Patient 4	Total sample Mean (SD)
Age at rTMS (years)	38	33	34	36	35.2 (2.2)
Week of gestation at symptom onset	4	4	6	6	5 (1.2)
Week of gestation at rTMS initiation	4	6	10	8	7 (2.6)
Antidepressant use before rTMS (weeks)	52	32	12	N/A	32 (20)
Previous major depressive episodes (n)	2	1	1	1	1.25 (0.5)
HDRS-21 score					
Before rTMS	29	27	12	17	21.2 (8.1)
After rTMS	13	4	6	5	7.0 (4.1)
Relative change (%)	-55.2	-85.2	50.0	-70.6	-65.3 (15.9)
HARS-14 score					
Before rTMS	42	15	28	20	26.3 (11.8)
After rTMS	19	3	12	6	10.0 (7.1)
Relative change (%)	-54.8	-80.0	-57.1	-70.0	-65.5 (11.8)
CGI-S score					
Before rTMS	5	6	5	5	5.3 (0.5)
After rTMS	2	1	2	2	1.8 (0.5)
Relative change (%)	-60.0	-83.3	-60.0	-60.0	-65.8 (11.7)
Characteristics of rTMS treatment					
DLPFC side	Left	Left	Right	Left	
Sessions (n)	50	38	20	40	37.0 (12.5)
Pulses (× 1,000)	150	114	36	120	105.0 (48.6)
% of motor threshold	120	120	120	120	
Concomitant pharmacotherapy	Yes	Yes	Yes	No	3.0 (75.0)
Antidepressant	Sertraline	Sertraline	Fluoxetine		
Daily dosage	150 mg	150 mg	40 mg		
Concomitant psychotherapy	No	Yes	Yes	No	2.0 (50.0)
Technique		CBT	PP		
Duration of therapy before rTMS (weeks)		12	36		
Family history of depression	Yes	No	Yes	Yes	3.0 (75.0)
Current psychiatric comorbidity	None	OCPD	None	None	1.0 (25.0)
Previous psychiatric comorbidity	None	None	Alcohol abuse and BD-II	None	1.0 (25.0)
Side effects of rTMS					
Pain/discomfort at the application site	No	Yes	Yes	Yes	3.0 (75.0)
Transient difficulty in concentration	Yes	No	No	No	1.0 (25.0)
Sore throat	No	No	Yes	No	1.0 (25.0)

BD-II = bipolar disorder type II; CBT = cognitive behavioral therapy; CGI-S = Clinical Global Impression-Severity; DLPFC = dorsolateral prefrontal cortex; HARS-14 = 14-item Hamilton Anxiety Rating Scale; HDRS-21 = 21-item Hamilton Depression Rating Scale; N/A = not applicable; OCPD = obsessive-compulsive personality disorder; PP = psychodynamic psychotherapy; rTMS = repetitive transcranial magnetic stimulation.

Disclosure

The authors report no conflicts of interest.

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