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LETTERS TO THE EDITORS

Discriminant analysis of caregivers' psychiatric symptoms according to offspring psychopathology

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Associations between parent or caregiver depression and adverse child outcomes are well established.[1] We previously examined correlations of symptoms of common mental disorders in caregivers with offspring psychopathology in a Brazilian sample.[2] Sixty-eight primary caregivers of 110 children (age 6-15 years) were enrolled. Caregivers were assessed using the Self-Reporting Questionnaire[3] (SRQ-20), which measures symptoms of common mental disorders. We used the Strengths and Difficulties Questionnaire (SDQ) to measure children's symptoms. In our previous results, higher SRQ-20 scores in caregivers correlated significantly with offspring psychiatric symptoms (beta = 0.20; p = 0.04).

We further investigated this result by conducting a discriminant analysis. A multinomial logistic regression with Bayesian estimation (Mplus, 7.4) was carried out to identify the symptoms assessed with the SRQ-20, discriminating three groups of children: 1) asymptomatic (SDQ $<$ 14, impact supplement score = 0); 2) symptomatic without impact (SDQ $\geqslant$ 14, impact supplement score = 0); and 3) symptomatic with impact (SDQ $\geqslant$ 14, impact supplement score $\geqslant$ 1).

The results (Table 1) showed that caregivers of symptomatic children without impact reported lower depressed mood, lower somatic (anxiety) and somatic (gastrointestinal) symptoms, more weight loss, and lower insight compared to caregivers of asymptomatic children. Caregivers of symptomatic children with impact reported lower depressed mood, lower retardation, more agitation, lower somatic (gastrointestinal) symptoms, more weight loss, and less insight than caregivers of asymptomatic children. Comparison between the two groups of caregivers of symptomatic children showed that the group with impact reported higher levels of early insomnia, lower retardation, lower agitation, higher anxiety (psychological and somatic), more somatic symptoms, and less insight.

These results possibly demonstrate a trend toward symptomatology interaction between caregivers and their offspring. Weissman et al. studied the differential effects of a depressed mother's treatment on her child, and found that children whose mothers were on escitalopram showed significantly greater improvement in symptoms and functioning as compared to children whose mothers were on bupropion or a combination of both.[4] The authors also observed that maternal baseline negative affectivity (which captures high levels of stress, irritability, and anxiety) appeared to moderate the effect of maternal treatment on children. Possibly, these mothers are better treated with escitalopram, which enhances serotoninergic neurotransmission, as compared to bupropion, which enhances dopaminergic transmission.

In another study, Morgan et al. evaluated how maternal neural response to child affect is related to depression by using an fMRI task.[5] They found that comorbid anxiety, chronicity of depression, and poor mother-child relationship emerged as predictors of altered maternal neural response to child affect. Few studies have sought to elucidate the mechanisms of parental-offspring psychopathology.

Table 1 Results of multinomial logistic Bayesian regression analysis

	SDQ- vs. SDQ+ without impact		SDQ- vs. SDQ+ with impact		SDQ+ without impact vs. SDQ+ with impact	
	Beta	*p*-value	Beta	*p*-value	Beta	*p*-value
Depressed mood	**-0.25**	**0.04**	**-0.32**	**0.03**	-0.18	0.11
Feelings of guilt	0.25	0.09	0.18	0.09	0.20	0.06
Suicide	-0.19	0.15	-0.13	0.17	0.21	0.07
Insomnia, early	-0.30	0.09	0.09	0.32	**0.46**	**0.00**
Insomnia, middle	0.38	0.06	0.01	0.48	-0.08	0.30
Insomnia, late	-0.13	0.32	0.01	0.50	-0.15	0.19
Work and activities	0.04	0.43	0.07	0.34	-0.08	0.31
Retardation, psychomotor	0.01	0.47	**-0.34**	**0.02**	**-0.22**	**0.03**
Agitation	0.28	0.08	**0.44**	**0.01**	**-0.40**	**0.01**
Anxiety (psychological)	0.20	0.15	0.24	0.06	**0.40**	**0.01**
Anxiety (somatic)	**-0.32**	**0.02**	-0.13	0.21	**0.32**	**0.01**
Somatic symptoms (gastrointestinal)	**-0.54**	**0.01**	**-0.40**	**0.03**	0.27	0.09
Somatic symptoms (general)	-0.06	0.34	-0.04	0.38	**0.27**	**0.01**
Genital symptoms	-0.00	0.50	-0.08	0.30	-0.19	0.07
Hypochondriasis	0.07	0.35	0.00	0.50	-0.18	0.08
Weight loss	**0.54**	**0.00**	**0.53**	**0.01**	-0.21	0.09
Insight	**-0.34**	**0.00**	**-0.26**	**0.02**	**0.20**	**0.04**

SDQ = Strengths and Difficulties Questionnaire applied to children; SRQ-20 = Self Reporting Questionnaire-20 applied to adult caregivers; SDQ- = asymptomatic children (SDQ $<$ 14); SDQ+ = symptomatic children (SDQ $\geqslant$ 14); impact = symptomatic children with impact supplement score $\geqslant$ 1.
Bold font indicates statistical significance.

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.

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The authors report no conflicts of interest.

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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*.

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