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LETTERS TO THE EDITOR

Seasonal and temperamental contributions in patients with bipolar disorder and metabolic syndrome

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Dear Editor,

I read with interest the article by Altinbas et al. (in this issue) suggesting that the prevalence of the metabolic syndrome in individuals with bipolar disorder is influenced by seasonality, with higher rates reported in the winter and spring months. They further opine that temperamental dimensions (e.g. depression) constitute a vulnerability factor to the seasonal influence. The article is appropriate in highlighting that their small sample size, open label design and absence of a control group, among other limitations, affect the inferences that can be drawn from their outcome. Their paper is hypothesis-generating rather than hypothesis-confirming.

The authors remind us that environmental factors (e.g. seasonality) affect susceptibility to allostatic load. It is amply documented that bipolar symptoms/episodes are affected by seasonality in susceptible subsets. It could be conceptualized that metabolic syndrome (e.g. obesity) is a phenotypic manifestation of an abnormal stress response with somatic manifestations. It would be interesting to know whether individuals with metabolic syndrome seasonality are more or less likely to also experience breakthrough symptomatology.

There is tremendous interest in conceptualizing bipolar disorder as progressive disorders.[1] I would conjecture that obesity and associated metabolic abnormalities are a cause and consequence of progression in bipolarity.[2-4] Indeed, this remains a testable hypothesis. My clinical impression is that individuals with bipolar disorder who exhibit susceptibility to symptomatic recurrence as a function of seasonality often present with ''mixed presentations.''[5] It is tempting to further speculate that obesity, which is depressogenic, may be affecting the symptomatic presentation of bipolar disorder, increasing the likelihood that these patients will present as ''mixed.'' Again, my clinical impression is that bipolar patients that I have encountered over the last decade are more often mixed than they are euphoric, and I have wondered whether, in addition to the inappropriate use of antidepressants, obesity is changing the ''face'' of bipolar disorder.

I further applaud the authors for reminding us of possible temperamental contributions and giving us a ''dose of reality'' that there will be no unidimensional explanation for psychiatric disorders that is coherent, comprehensive, and explanatory.

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Disclosure

The author reports no conflicts of interest.

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rTMS as an add-on treatment for resistant obsessive-compulsive symptoms in patients with schizophrenia: report of three cases

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Dear Editor,

Obsessive-compulsive symptoms (OCSs) occur in approximately 30% of patients with schizophrenia, probably reflecting reduced basal ganglia and prefrontal cortex connectivity, and are associated with poorer prognosis.[1] There is little systematic evidence of treatment effect on OCS schizophrenia, mostly derived from case reports and open label uncontrolled studies. Among new treatments, repetitive transcranial magnetic stimulation (rTMS) is a method of noninvasive electromagnetic neurostimulation that has demonstrated effect on verbal hallucinations and depressive symptoms.[2,3] Nevertheless, contradictory effects on obsessive-compulsive disorder

Table 1 Results obtained in the three cases

Patient	Age, y	Illness duration, y	Gender	DSM-IV diagnosis	Medication used	Y-BOCS			BPRS		
						T1	T2	T3	T1	T2	T3
1	42	25	F	SZ	Clozapine 400 mg Citalopram 40 mg	33	24	29	15	10	11
2	27	9	M	SZA	Clozapine 600 mg Valproate 2000 mg	17	11	21	4	2	3
3	30	15	M	SZ	Clozapine 600 mg Valproate 1500 mg Amitriptyline 125 mg	24	23	24	32	11	26

BPRS = Brief Psychiatric Rating Scale; SZ = schizophrenia; SZA = schizoaffective disorder; y = years; m = male; f = female; T1 = baseline; T2 = after 20 repetitive transcranial magnetic stimulation sessions; T3 = 4 weeks after treatment cessation; Y-BOCS = Yale-Brown Obsessive Compulsive Scale.

(OCD) have been reported,[2,4] depending on the stimulation parameters used (frequency, place, total dose). Furthermore, there has been some evidence of effects on compulsions using the Mantovani's protocol (1 Hz over the supplementary motor area - SMA),[5] whilst dorsolateral prefrontal cortex failed to reveal consistent effect even at low or high frequency, and right or left hemisphere.

We report on three cases of comorbid schizophrenia or schizoaffective disorder and OCS under stable dose of neuroleptics receiving additional rTMS with the Mantovani protocol (1 Hz, SMA, 100% of motor threshold, 20 minutes, 20 sessions in 4 weeks), showing reduced OCSs after rTMS treatment. The protocol was approved by the Ethics Committee of the HCPA (Hospital de Clínicas de Porto Alegre - GPPG 10-0426), and patients and relatives provided informed consent.

All cases had treatment-resistant schizophrenia (n=2) or schizoaffective disorder (n=1) with at least 3 months under stable dose of clozapine. Diagnosis was based on the DSM-IV-TR criteria administered by the same trained psychiatrist (VMF) and reviewed by a senior psychiatrist (MIRL). Psychopathology was measured by the 18-item Brief Psychiatric Rating Scale (BPRS) and the Yale-Brown Obsessive Compulsive Scale (Y-BOCS). The characteristics of the three cases are described in Table 1. All subjects displayed improvement on the BPRS and OCD symptoms after the add-on rTMS treatment, but with subsequent relapse after 4 weeks (Table 1).

As far as we are aware, this is the first report of the effects of add-on rTMS on the treatment of OCSs in refractory schizophrenia. These three cases provide initial evidence for the use of the Mantovani protocol (SMA) in this group of patients, in addition to previous effects of rTMS on auditory hallucinations.[2,3]

This report must be viewed as initial evidence requiring further studies with larger number of cases and double-blind sham control group. The number of cases (n=3) precluded statistical testing and displayed relatively large age, gender and diagnosis heterogeneity. Nevertheless, despite the limitations that hinder further generalization, patient diagnosis and psychopathology were consistently assessed, and cases had no significant variations in terms of drug dose and psychosocial environment over the observational period. This reinforces the need of additional studies with larger sample size, less variability of age, gender and diagnosis, longer follow-up, and use of additional tools (functional magnetic resonance imaging-positron emission tomography, fMRI-PET) to elucidate efficacy, duration, and underlying mechanisms of action of the rTMS treatment[5] in comorbid schizophrenia-schizoaffective disorder-OCS.

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The authors report no conflicts of interest.

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