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Research report

Seasonal pattern of manic episode admissions among bipolar I disorder patients is associated with male gender and presence of psychotic features

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ABSTRACT

Background: Bipolar I disorder (BD-I) patients demonstrate disrupted chronobiology expressed as seasonal variation in mood symptoms. The seasonal pattern (SP) specifier of mood disorders was recently extended by the DSM-5, to be applied to manic episodes. However, the significance of seasonality of manic episodes for the course of BD-I is unknown. In the present study we sought to identify clinical and demographic features that discriminate between BD-I patients with and without SP of manic admissions. **Methods:** BD-I patients ($n=148$) admitted at least twice with the same mood exacerbation type, were retrospectively followed between 2005 and 2013. Demographic and clinical characteristics were compared between BD-I patients with or without SP of manic admissions.

Results: SP of manic episode admissions, found in 31 (26%) of 117 BD-I patients with repeated manic episode admissions, was associated with higher rates of male gender ($p=0.01$), presence of psychotic features ($p=0.01$) and comorbid substance use disorder ($p < 0.05$) compared to patients without SP. In a multivariate analysis, SP of manic episode admissions was associated with the presence of psychotic features (OR 8.42, 95% CI: 1.05–67.65, $p < 0.05$) and male gender (OR 3.23, 95% CI: 1.08–9.65, $p < 0.05$), but not with comorbidity of substance use disorder (OR 1.79, 95% CI: 0.71–4.50, $p=0.24$).

Limitations: Seasonal psychological/environmental factors contributing to the emergent of mood episodes could not be ruled out.

Conclusions: Our results suggest that SP of manic admissions is associated with male gender and the presence of psychotic features, thus might be associated with more severe form of the disorder.

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1. Introduction

Accumulating data support the hypothesis that disrupted chronobiology may represent a core element of bipolar disorder (BD) and might play a role in the pathophysiology of this disorder (Salvatore et al., 2012; Scott, 2011). BD patients demonstrate irregular chronobiology expressed as disrupted sleep and circadian rhythms and greater seasonal fluctuations in mood and behavior compared to unipolar depression patients or healthy controls (Geoffroy et al., 2014). Seasonal variability of symptoms among BD patients and its significance for the course of the disorder were traditionally studied by exploring the seasonal distribution of admissions rates of BD patients and the association between

seasonal pattern (SP) of acute bipolar mood episode with specific clinical and demographic characteristics (Geoffroy et al., 2014).

According to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR), SP was restricted to depressive episodes. Consequently, in the past decades, SP was mostly studied for depressive episodes, and was found among 25% of BD patients. SP of depressive episodes among BD patients was found to be associated with bipolar II disorder (BD-II), rapid cycling, depressive onset and depressive predominant polarity, while data regarding gender differences according to SP are inconclusive (Arnold, 2003; Friedman et al., 2006; Goikolea et al., 2007). Previous studies using DSM-III criteria for SP, that were applied for both depressive and manic episodes, have identified around 15% of BD patients with SP of manic episodes and these patients presented more severe clinical profile (Geoffroy et al., 2014; Hunt et al., 1992).

Recognizing the accumulating data supporting the presence of SP both in manic and depressive episodes, the SP specifier of mood

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disorders was extended by the DSM, Fifth Edition (DSM-5) to be applied to manic/hypomanic episodes (American Psychiatric Association, 2013). However, data regarding the significance of manic episode seasonality for the course of BD are scarce. In the current study we aimed to identify clinical and demographic features that discriminate between bipolar I disorder (BD-I) patients with and without SP of manic episode admissions.

2. Methods

2.1. Population

We conducted a retrospective cohort study, using electronic medical records (EMR) review of all consecutive admissions to Geha Mental Health Center (GMHC, Petach Tikva, Israel) between January 1, 2005, and July 31, 2013. GMHC is a tertiary care referral mental health center that provides psychiatric care to more than 1500 patients admitted annually. The center serves a population of about 450,000. Patients are referred to the center by general practitioners, outpatient psychiatrists or are self-referred and all of them are admitted through the emergency room.

Out of 6084 patients admitted during the study period we identified 540 patients diagnosed as having DSM-IV-TR BD-I or BD-II according to the EMR review. The type of psychiatric exacerbation leading to each admission was classified as DSM-IV-TR manic, major depressive or mixed episode as established by a consensus of two senior psychiatrists following a psychiatric interview during the time of each hospitalization. To avoid confounding effects we excluded from the study mood episode admissions that were attributed to a substance use or a medical condition as well as patients under 18 years of age. Furthermore, BD-II patients were excluded from this study for two reasons: first, small number of patients and second, a higher probability for subthreshold hypomanic symptoms that might increase selection bias errors.

In order to determine a SP for each type of mood episode (manic, major depressive or mixed), only patients with repeated admissions (at least two) of the same type of mood episode, during the study period, were included in the study. Subsequently, BD-I patients were sub-grouped according to the type of the repeated mood episodes leading to admission (repeated manic episodes group, repeated major depressive episodes group and repeated mixed episodes group). The total number of patients included in the study was 148 with 402 repeated admissions due to acute mood episodes. Five of the patients met the inclusion criteria for more than one type of repeated mood episodes group (i.e., had at least two admissions for each type of mood episode, either depressive or manic) and were included in both types of repeated mood episodes group (Table 1). To differentiate among separate episodes in a patient with multiple admissions, we included in the study only the first admission if the patient had been readmitted within an 8-week period unless the polarity was reversed, in such cases both admissions were included (Lee et al., 2007). The study was approved by the GMHC Review Board.

2.2. Measures

Demographic and clinical data were collected retrospectively from the patients' EMR. Demographic data included age at first admission during the study period and gender. Clinical data included number of admissions per year during the study period, the type of mood episode leading to each admission (as described above), the presence of psychotic features during each mood episode (either delusions or hallucinations during the mood episode according to DSM-IV-TR), history of suicide attempt,

Table 1

Seasonal pattern and demographic characteristics [Mean \pm SD or N (%)] of Bipolar I disorder inpatients sub-grouped according to the type of repeated mood episodes leading to admission.

Characteristics	Type of repeated mood episodes group ^a		
	Repeated manic episodes group	Repeated major depressive episodes group	Repeated mixed episodes group
Number of patients	117	33	3
Number of admissions	313	83	6
Gender			
Female	41 (35%)	22 (67%)	2 (67%)
Male	76 (65%)	11 (33%)	1 (33%)
Age (yrs) ^b	36.8 \pm 14.8	51.6 \pm 16.5	45.0 \pm 14.5
Patients with Seasonal pattern	31 (26%)	7 (21%)	1 (33%)

SD = standard deviation.

^a Patients with repeated (at least two) admissions of the same type of mood episode (manic, major depressive or mixed) were classified according to the type of repeated mood episodes leading to admission.

^b Age (yrs) at first admission during the study period.

psychiatric comorbidities including substance use disorder, anxiety disorders and personality disorders (according to DSM-IV-TR criteria) and the type of psychotropic drugs at discharge from the hospital after the last admission.

For each patient, the presence of SP was determined, in a retrospective approach, separately for each type of a repeated mood episode leading to admission (manic, major depressive or mixed) according to DSM-5 criteria (consisting of temporal relationship between the time of repeated admissions of specific type of mood episode and a particular time (season) of the year, seasonal mood episodes substantially outnumber non-seasonal mood episodes during the study period and in the last two years of the study there have been only seasonal episodes). The season for each mood episode admission was determined according to admission date. Importantly, the SP was not determined for specific season but for each patient according to the time of repeated admissions. The duration of the various Israeli seasons were defined as follows: Winter: December–February; Spring: March–May; Summer: June–September; Fall: October–November (Shapira et al., 2004).

2.3. Statistical analysis

SPSS ver. 20 (SPSS inc, Chicago, IL) was used for statistical analysis. Descriptive statistics were expressed as Mean \pm SD, or rate (%). Demographic and clinical characteristics were compared between BD-I patients with or without SP of admissions (for each type of repeated mood episodes). Contingency tables were used to compare rates of gender, presence of psychotic features, history of suicide attempt, psychiatric comorbidities and type of psychotropic drugs at discharge from the hospital. Independent Student's *t*-test was used to compare age at first admission during the study period and the number of admissions per year. Differences in seasonal distribution of mood episode admission rates were analyzed by one-way ANOVA (Shapira et al., 2004). A logistic regression analysis was conducted with SP of manic episode as a dependent variable (dichotomous) and the presence of psychotic features, male gender and a substance use disorder as covariates. Odds ratios, 95% confidence interval and statistical significance were calculated. P value of <0.05 was considered statistically significance.

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