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The Relationship Between Bipolar Disorder, Seasonality, and Premenstrual Symptoms

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Abstract

Cyclical mood disorders characterized by shifting affective states include bipolar disorder, seasonal affective disorder, and premenstrual syndrome/premenstrual dysphoric disorder. In this article, we explore the relationship between these disorders and bring the reader up to date on the advances made in the past year in understanding the relationship between bipolar disorder, seasonality, and premenstrual symptoms.

Keywords

Bipolar disorder; Seasonality; Seasonal affective disorder; Women's health; Premenstrual syndrome; Premenstrual dysphoric disorder; Melatonin

Introduction

Cyclical mood disorders characterized by shifting affective states include bipolar disorder (BD), seasonal affective disorder (SAD), and premenstrual syndrome/premenstrual dysphoric disorder (PMS/PMDD). Researchers have hypothesized that there may be common biopsychosocial mechanisms underlying these disorders, as BD patients may have a greater degree of seasonality and premenstrual symptoms compared with patients with noncyclical mood disorders. Despite the reasonable hypothesis that these disorders are related, there are surprisingly sparse data available regarding this putative relationship, especially with regard to prospective studies that confirm patient self-reporting of seasonal and premenstrual symptomatology. In this review, we bring the reader up to date on the advances made in the past year in understanding the relationship between bipolar disorder, seasonality, and premenstrual symptoms.

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Bipolar Disorder and Seasonality

Seasonality can refer to the seasonal, circadian pattern of individual bipolar symptoms as well as to the co-occurrence of SAD with BD. Studying seasonality can be difficult due to the effects of geography and medications on symptoms. Seasonality can affect up to 20% to 25% of patients with BD and is more commonly reported in patients with BD II and with depressive episodes [1–3]. Data regarding the pattern of seasonal symptoms have been mixed, with some studies showing that relapse is more common in the fall and winter, and others showing no such seasonal pattern [4].

A recent cross-sectional study of 105 BD I and BD II outpatients evaluated multiple clinical characteristics, including seasonality, which was defined by the researchers as “a tendency to experience seasonal variations in mood behavior and vegetative functions.” A higher proportion of BD II patients reported seasonality (63.6%) compared with BD I patients (41.4%) (P=0.035) [5]. Although this study did not use a standardized seasonal symptom rating scale, another study by the same group did so [6•]. In this outpatient study, seasonal symptoms were retrospectively assessed using the Seasonal Pattern Assessment Questionnaire, which is calculated to determine the Global Seasonality Scale. Bipolar patients had a higher degree of seasonality (P=0.001) than controls, although there was no difference by BD type. Also, 15% of the bipolar patients met criteria for a comorbid diagnosis of SAD, although it was not stated which seasons patients perceived to be most difficult.

In another recent cross-sectional study comparing a bipolar and a primary care cohort, the bipolar group had 3.7-fold increased odds of having a self-reported diagnosis of SAD (using the Seasonal Pattern Assessment Questionnaire) [7]. BD patients were more likely to report seasonal fluctuations in mood, socializing, sleep, and weight [8]. In the BD group, the mean difference in sleep time between winter and summer was 1.8 h (less sleep in summer), compared with 1 h in the primary care sample. It would be interesting to determine how seasonality as rated by clinicians would affect these numbers. It is also unclear what impact gender has on seasonality in BD. However, it is clear that seasonality is an important part of the clinical presentation of BD. Patients initially diagnosed with SAD can, upon careful questioning, actually be subsequently diagnosed with BD [9] because bipolar patients often have atypical depressive symptoms that are commonly seen in SAD [10]. Given that bipolar depressive episodes can be difficult to treat, some authors are recommending that light therapy be considered for bipolar patients with consistent depressive symptoms during fall and winter [8, 9, 11, 12]. This should be done cautiously, and monitoring for hypomania/mania is necessary, but it is likely safe, although efficacy results are preliminary.

Bipolar Disorder and Premenstrual Symptoms

To date, there are no consistent data linking the pattern of affective changes in women with BD, and the menstrual cycle and premenstrual symptoms do not show familial aggregation in families with BD [13, 14]. Nevertheless, 60% to 70% of women with BD self-report premenstrual exacerbation of their symptoms [15•, 16]. In a recent longitudinal study of 293 women with BD, bipolar women with retrospectively self-reported premenstrual

exacerbation had a worse course of illness when observed prospectively, with more mood symptoms (mainly depressive) than bipolar women without premenstrual exacerbation [15•]. However, they were not more likely to have a diagnosis of rapid cycling BD. In another study, 25 of 92 (27%) women consecutively enrolled with BD reported a lifetime diagnosis of PMDD according to the DSM-IV criteria. PMDD was more common in women with BD II subtypes and in women who reported a history of postpartum depression. Incidentally, 35% to 40% of this cohort reported seasonality, but this did not differ by PMDD status. Finally, in a cross-sectional study examining 61 patients with BD compared with 122 age-matched, healthy controls, 74.9% of the BD patients self-reported severe PMS symptoms, compared with 19.7% of controls (P=0.001). There was also a significant difference in the occurrence of PMDD (29.3% vs 1.6%; P<0.0001). For both PMS and PMDD, the highest frequency was seen in BD II patients. This study did show a significant association between PMS and seasonality (F=4.83, P=0.029). In sum, all these studies have employed self-report, retrospective tools to assess premenstrual symptoms that may overestimate the rates of these symptoms in bipolar women. The treatment of PMS/PMDD in bipolar women is of considerable interest because oral contraceptives and serotonin reuptake inhibitors can influence affective states. No studies have formally tested the use of mood stabilizers or antipsychotics in the treatment of PMS/PMDD.

Bipolar Disorder and Melatonin

An important potential biological link between cyclical affective phenomena such as BD, seasonality, and premenstrual symptoms is the hormone melatonin (N-acetyl-5-methoxytryptamine), which is secreted from the pineal gland located near the center of the brain. In the pineal gland, serotonin is acetylated and then methylated to produce melatonin. Melatonin responds to external light conditions to regulate the circadian rhythm. Melatonin levels are generally lower during daytime hours compared with night. The onset, offset, and duration of melatonin secretion has been found to be altered in BD patients and individuals with SAD. External light sources significantly suppress melatonin secretion in BD patients compared with controls [17–19]. This increased sensitivity is not state dependent, as it occurs over the manic, depressed, and euthymic phases of the illness [17, 20]. Both valproate and lithium decrease the sensitivity of melatonin to light, which may relate to their therapeutic effect in BD by lengthening the circadian period [21, 22]. A similar sensitivity to light-induced melatonin suppression occurs in SAD and PMDD, which is one rationale for testing the efficacy of lithium in patients with PMDD [23].

Bipolar Disorder and the Postpartum Period

Women with premenstrual symptoms may be more likely to experience postpartum depression [24]. In addition, women with BD are at significantly increased risk of psychiatric admission in weeks 2 to 3 postpartum compared with women without BD [25]. New data suggest that more than 50% of the cases of postpartum depression unresponsive to a single antidepressant trial are later diagnosed as BD [26]. Of this cohort, the most common medication change was to add or switch to a second-generation antipsychotic. Up to 15% of postpartum women experience hypomanic symptoms in the immediate postpartum period, but it is unclear which of these women will go on to receive a BD diagnosis [27]. Screening

for BD in the postpartum period is an understudied area of research. A recent study evaluated the sensitivity and specificity of the Mood Disorders Questionnaire as a screening instrument in 125 women with BD or major depressive disorder at 2 to 4 weeks postpartum [28]. Using the traditional scoring system (seven or more symptoms), although 46% of the sample had a BD diagnosis, only 30% of women were identified. Using eight or more symptoms improved the sensitivity and specificity of the Mood Disorders Questionnaire (87.72% and 85.29%, respectively). It may be of value to add a bipolar screening to the screening for postpartum depression. Certainly in women with continued symptoms despite an adequate antidepressant trial or in women with a first-degree relative with BD, a bipolar diagnosis should be strongly considered in the postpartum period. The risk of missing a bipolar diagnosis cannot be underestimated given that the most common diagnosis in women with postpartum psychosis is actually BD [29].

Conclusions

Women with BD commonly report seasonal and premenstrual symptoms based on retrospective self-report of symptoms. This may overestimate the prevalence; therefore, the field needs more prospective trials in which clinicians rate the symptoms over time. There may be a shared endophenotype, such as an increased sensitivity to light-induced melatonin suppression, but this has yet to be fully delineated. In bipolar patients, clinicians should more carefully evaluate seasonality and premenstrual symptoms because patients with these comorbidities may have a more treatment-resistant course. Postpartum episodes are underrecognized as presentations of BD, and clinicians should screen for mania, hypomania, and a family history of BD when screening for postpartum depressive symptoms. Few data are available with regard to how to treat seasonal and premenstrual exacerbations, although phototherapy may be an option for fall/winter exacerbation of depressive symptoms.

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