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Seasonal variation of manic and depressive symptoms in bipolar disorder

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Abstract

Objectives—Analyses of seasonal variation of manic and depressive symptoms in bipolar disorder in retrospective studies examining admission data have yielded conflicting results. We examined seasonal variation of mood symptoms in a prospective cohort with long-term follow-up: The Collaborative Depression Study (CDS).

Methods—The CDS included participants from five academic centers with a prospective diagnosis of bipolar I or II disorder. The sample was limited to those who were followed for at least 10 years of annual or semi-annual assessments. Time series analyses and autoregressive integrated moving average (ARIMA) models were used assess seasonal patterns of manic and depressive symptoms.

Results—A total of 314 individuals were analyzed [bipolar I disorder: (n = 202) and bipolar II disorder: (n = 112)] with both disorders exhibiting the lowest depressive symptoms in summer and highest around the winter solstice, though the winter peak in symptoms was statistically significant only with bipolar I disorder. Variation of manic symptoms was more pronounced in bipolar II disorder, with a significant peak in hypomanic symptomatology in the months surrounding the fall equinox.

Conclusions—Significant seasonal variation exists in bipolar disorder with manic/hypomanic symptoms peaking around the fall equinox and depressive symptoms peaking in months surrounding the winter solstice in bipolar I disorder.

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Keywords

bipolar I disorder; bipolar II disorder; depression; hypomania; mania; seasonal variation

It is not clear whether a seasonal pattern exists in the psychopathology of bipolar disorder. The current literature is populated mainly with retrospective studies of admission data for individuals with discharge diagnoses of bipolar disorder. Mood episodes appear more likely to be exacerbated in the spring when analyzing hospital admissions as well as self-reported depression measures (1–3). The peak in admissions for mania has been found in the spring, summer, or both (4–6). Another retrospective study found a lack of seasonal pattern in hospital admissions for bipolar disorder (7).

Depressive symptoms have more consistently shown peaks in the spring and autumn (8, 9). A study examining hospital admission data reported that bipolar depression shows seasonality which peaks in the months of June and July (4). In each of these studies, individuals with bipolar I and II disorder were not compared. This is significant since people with bipolar II disorder often exhibit a greater chronicity of illness than do those with bipolar I disorder (10); thus, it is plausible that the seasonality of bipolar I disorder and bipolar II disorder may differ and should be examined separately. As a result, studies examining seasonality between bipolar I and bipolar II disorder are of particular relevance.

A retrospective study examining admission statistics for bipolar depression and mania found that participants with bipolar I depression were mainly hospitalized in summer and winter, whereas for bipolar II depression, most admissions for depression occurred in the spring and summer. Admission for mania peaked in spring and autumn (11). Another study that included a four-year retrospective component with prospective follow-up for two years demonstrated that relapse of mania did not show a seasonal pattern, but bipolar depression demonstrated a significant peak in autumn (12), while endogenous and neurotic depression peak in the spring (13). Manic and depressive relapses were measured with the use of two cohorts of bipolar I disorder participants selected based on a case-note search of admission to the psychiatric services at each locality from 1985–1987, with diagnosis confirmed after an initial assessment interview using the Schedule for Affective Disorders and Schizophrenia (SADS) (14). Though this is the only study that included prospective follow-up, limitations included a small sample size, with only 144 individuals fulfilling criteria and follow-up of two years (15).

Retrospective studies examining seasonality of bipolar depression and mania have been limited to data on hospitalizations or retrospective report that may be subject to undue recall bias. As a result, another valuable approach to determining the seasonality of bipolar I and II disorder would be to examine prospective studies. In addition, existing studies are limited by sample size and duration of follow-up, and by reliance on admission statistics to determine a seasonal pattern. A spectrum of symptoms exists in mood disorders and most do not reach a threshold of severity wherein hospitalization would be required.

Studies examining frequency of symptoms of bipolar I disorder versus bipolar II disorder have demonstrated that bipolar II disorder individuals spend a significantly higher

percentage of weeks exhibiting depressive symptoms than do those with bipolar I disorder, with both disorders expressing more depressive symptoms than manic/hypomanic symptoms (10, 16). An examination of 1,000 patients from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) throughout the course of a year found that bipolar II disorder individuals were more ill year-round and exhibited a significantly greater monthly fluctuation prevalence rate of symptoms than bipolar I disorder participants (17). Subsyndromal symptoms are common and not all syndromal individuals require hospitalizations; thus, analyzing only admissions statistics may overlook less severe, but clinically significant psychopathology.

Self-reported mood ratings capture these less severe, but clinically significant symptoms. Symptoms that are subsyndromal in duration or intensity are common in the longitudinal course of bipolar disorder (19, 20). One study of 360 patients with bipolar disorder, who recorded their mood daily, did not demonstrate a seasonal pattern for depressed and hypomanic/manic episodes (18). Relying solely on self-report has its limitations, such as reliance on insight into a manic episode (21). Self-reported mood studies in bipolar disorder have also been limited by duration of follow-up and sample size.

We sought to assess seasonal variation in manic and depressive symptoms in bipolar disorder utilizing a long-term prospective cohort study: The Collaborative Depression Study (CDS). Our study includes prospective follow-up for at least 10 years, which is longer than any other prospective study duration. The objectives of our study were to determine if seasonal variation exists in bipolar disorder with examination of a seasonal variable in symptom burden measures, and timing of relapse for depressive as well as manic/hypomanic/mixed episodes. We additionally sought to identify differences in seasonality by bipolar subtype.

Methods

Participants

The CDS included individuals with mood disorders from the following academic centers: Harvard University (Boston, MA, USA), Rush Presbyterian-St. Luke's Medical Center (Chicago, IL, USA), University of Iowa (Iowa City, IA, USA), New York State Psychiatric Institute and Columbia University (New York City, NY, USA), and Washington University School of Medicine (St. Louis, MO, USA). All centers are in temperate regions of the contiguous United States (38.75–42.37 degrees latitude), although participants did not necessarily reside in these regions throughout follow-up. The institutional review boards of all sites approved the study and all participants provided written informed consent.

All participants included in this study underwent an initial assessment with the use of the Schedule of Affective Disorders and Schizophrenia (SADS) scale to determine if they met Research Diagnostic Criteria (RDC) for major depressive disorder, schizoaffective disorder, or manic disorder (14, 22). Treatment was neither required nor administered by study staff in this observational study.

We included individuals with a prospective diagnosis of bipolar disorder based on prior methods (16, 23). The CDS used RDC criteria (the progenitor of DSM-III) in which schizoaffective, mainly affective, are consistent with a DSM-IV defined primary mood disorder. We restricted the sample size further to include only those participants with at least 10 years of follow-up to facilitate a 10-year time series analysis and to maximize our ability to identify seasonal patterns over long-term follow-up. For example, if we had chosen to allow a minimum of two years of follow-up, there might have been participants included in our dataset who had only approximately eight weeks of data for a given month, which would not allow us to reliably estimate symptom burden by month within individuals. After exclusion, our analysis included 313 individuals (202 with bipolar I disorder and 112 with bipolar II disorder). Participants were Caucasian (genetic hypotheses were tested), spoke English, had an IQ score of at least 70, and had no evidence of terminal medical illness at intake nor a mood disorder due to a primary medical condition. Table 1 provides the sociodemographic and clinical characteristics of the sample by bipolar subtype at study entry.

Follow-up course

Individuals were interviewed every six months for the first five years of follow-up and then annually by trained raters who used the Longitudinal Interval Follow-up Evaluation (LIFE), a system for assessing longitudinal course, including an instruction booklet, coding sheet, and training materials to guide the interview (24). Semi-structured interviews were the primary source of information used in the LIFE data, and they assessed weekly symptom severity on ordinal scales. Patient interviews included chronological memory prompts to determine symptoms for mood disorders. Medical records, along with data obtained from interviews were quantified using the LIFE Psychiatric Status Rating (PSR) scales (Table 2 and Table 3), which directly correlate to the diagnostic thresholds of the RDC (10). Major depression was based on PSR ratings for major depression or schizoaffective disorder, depressive type (see Table 2). Mania was based on PSR ratings for manic disorder or schizoaffective disorder, manic type (see Table 2). Clinically significant symptoms could also be registered on the scales for hypomania, intermittent depressive disorders, and minor depressive disorder (Table 3).

Data analysis

We examined the seasonality of symptom burden in bipolar I disorder and bipolar II disorder, based on previously defined thresholds of ≥ 3 on the major depression/mania PSR scale (Table 2) or three out of three on the minor depression/hypomania PSR scale (Table 3) (16, 23, 25). In addition, we assessed whether the timing of relapse in individuals with bipolar I or bipolar II disorder demonstrated a seasonal pattern. For the latter, the unit of analysis was mood episode, rather than individual participant. The beginning of a cycle was determined by the first week of any recurrence following a period of recovery. Recovery was defined as eight consecutive weeks with no or only residual symptoms (PSR ≤ 2) on the major depressive, manic, schizoaffective depressive, or schizoaffective manic scales of the PSR with no symptoms on the hypomania, minor depression, or intermittent depression scales. The cycle ended the week prior to any recurrence (following a period of recovery) or the point at which the participant was lost to follow-up. A recurrent mood episode was

defined as any PSR scale > 2 lasting one or two weeks, for manic/hypomanic and depressive symptoms, respectively (23).

Time series analyses were performed on the percent of weeks by month that individuals with either bipolar I or bipolar II disorder experienced depressive symptoms, and on the percent of weeks by month that individuals with either bipolar I or bipolar II disorder experienced manic symptoms. We built autoregressive integrated moving average (ARIMA) models to investigate the seasonal patterns of the monthly data over 10 years. In the ARIMA models examining depression, an indicator for the winter solstice (designating the months before and after the solstice: November, December, and January) was included in the model as a binary regressor. However, in the ARIMA models examining mania, an indicator for the autumnal equinox (designating the months before and after the month of the equinox: August, September, and October) was included in the model. These month indicators were selected after reviewing the descriptive data and after initial ARIMA models without these three-month season indicators revealed significant seasonal ARIMA components. The effect estimates corresponding to these indicators represent the elevation in the average symptom burden during the three-month period of interest.

In a sensitivity analysis, we looked at percentage of weeks with manic and depressive symptoms in a subsample of individuals who had at least two consecutive years without antidepressants or electroconvulsive therapy (ECT) as previously defined (26). Seasonal patterns of the monthly data over 10 years were again investigated using ARIMA models based on the same indicators for winter solstice (depression) and the autumnal equinox (mania).

Results

As seen in Figure 1, and consistent with prior results in the full CDS sample (10, 16) individuals with bipolar II disorder ($n = 202$) spent a greater proportion of weeks (40.5%) with clinically significant depressive symptoms than participants with bipolar I disorder ($n = 112$) (31.5%). The quantitatively lowest proportion of weeks with clinically significant depressive symptoms were in the months of July (38.7%) and August (39.1%) for individuals with bipolar II disorder; whereas those with bipolar I disorder experienced the lowest proportion of weeks with clinically significant depressive symptoms in the months of July (30.5%) and October (30.5%). The greatest proportion of weeks with clinically significant depressive symptoms were in the months of December (42.1%) and January (42.0%) for participants with bipolar II disorder; whereas for bipolar I disorder, depressive symptom burden was greatest in January (32.3%) and February (32.3%). When both groups were analyzed together, the proportion of clinically significant depressive symptoms was lowest in July (33.4%) and August (33.7%), and highest in January (35.8%) and February (35.6%). The two-sided Wald tests analyzing depression illustrated the month indicator for patients with bipolar I disorder or bipolar II disorder had a p-value of 0.095. However, the p-value for patients with only bipolar I disorder was 0.048 [effect estimate = 0.0085, 95% confidence interval (CI): 0.0001–0.0169], and for patients with only bipolar II disorder the p-value was 0.87. Thus, only the patients with bipolar I disorder had a significant peak of severe depressive symptoms in the months of November, December, and January.

Figure 2 displays the proportion of clinically significant manic symptoms and, as expected (10), participants with bipolar I disorder on average experienced a greater proportion of weeks (10.7%) with clinically significant mood elevation than did those with bipolar II disorder (1.6%). Hypomanic symptoms in individuals with bipolar II disorder increased during the months surrounding the autumnal equinox, and peaked in August (2.2%) and September (2.4%). This did not appear as pronounced for individuals with bipolar I disorder. The two-sided Wald tests analyzing mania demonstrated the month indicator for patients with bipolar I or bipolar II disorder had a p-value of 0.0003 (effect estimate = 0.0061, 95% CI: 0.0028–0.0094). The p-value of participants with bipolar I disorder was 0.01 (effect estimate = 0.0062, 95% CI: 0.0015–0.0109), and for those with bipolar II disorder the p-value was 0.002 (effect estimate = 0.0060, 95% CI: 0.0023–0.0097). Thus, all patients with either bipolar I or bipolar II disorder exhibited a significant peak of severe manic symptoms in the months of August, September, and October.

We next examined whether relapses after recovery from the index episode demonstrated a seasonal pattern. Figure 3 illustrates the percentage of new major/minor depressive episodes by month in bipolar I and bipolar II disorder. In bipolar I and bipolar II disorder there were a total of 772 and 693 episodes of major depression, respectively. Depressive episodes in bipolar I disorder peaked in May (10.1%) and August (9.7%), with the lowest frequency of episodes in June (6.9%) and July (5.7%). Depressive episodes in bipolar II disorder peaked in October (11.3%) and November (10.8%), with the lowest percentage of episodes in February (6.4%) and March (5.6%).

Figure 4 illustrates the percentage of new manic/hypomanic or mixed episodes by month in bipolar I and bipolar II disorder. In bipolar I and bipolar II disorder there were 502 and 83 manic/hypomanic or mixed episodes, respectively. Mood-elevated episodes in bipolar I disorder were observed most commonly after remission in March (10.0%), July (9.4%), and October (9.4%), and less often in May (6.6%) and June (6.8%). Hypomanic episodes following remission in bipolar II disorder were most common in August (15.7%). There was a gradual increase in the percentage of manic episodes beginning in May that peaked in August in bipolar II disorder.

A total of 139 participants had two consecutive years without treatment in this first 10 years. These participants had a mean of 5.8 [median = 5.1; standard deviation (SD) = 2.8] years without treatment over this timeframe. Similar inferential results were observed for this group. The two-sided Wald tests analyzing depression demonstrated the month indicator for patients with bipolar I or bipolar II disorder had a p-value of 0.28 (effect estimate 0.0069, 95% CI: –0.0056 to 0.0194). The two-sided Wald tests analyzing mania demonstrated the month indicator for patients with bipolar I or bipolar II disorder had a p-value of 0.004 (effect estimate = 0.0054, 95% CI: 0.0017–0.0091).

Discussion

Individuals with bipolar disorder demonstrated evidence of seasonal variability, particularly with regard to manic/hypomanic symptomatology, which peaked in the months surrounding the autumnal equinox (August–October). Individuals with bipolar I disorder also had a

significant peak of severe depressive symptoms surrounding the winter solstice (November–January). Although analysis of new manic and mixed episodes in bipolar I disorder was less clear, individuals with bipolar II disorder demonstrated another clear peak for such episodes in August. This supports the prior suggestion of greater seasonality in bipolar II disorder than in bipolar I disorder (17) with peaks of hypomania in autumn confirmed by analysis of both symptom burden and new episode onset metrics. However, time series analysis of mania demonstrated that all patients with either bipolar I or bipolar II disorder exhibited a significant peak of severe manic symptoms during autumn. The less clear patterns observed when looking at new episodes likely reflect their relative infrequency given the rigorous remission criteria employed and the availability of symptom burden data for every patient each month.

Seasonal variability in depressive and manic episodes is a challenge to reliably ascertain. Our results demonstrate that the mania is highest around the autumnal equinox and lowest in winter months for both bipolar I and II disorder individuals when analyzing symptom burden. Our results are contrary to previous findings, however, our methods may account for such differences (7, 12). Both prior studies had components of retrospective and admission data analysis that may fail to capture lower, but still clinically significant, levels of symptomatology that do not require hospitalization. As mentioned above, studies have shown that bipolar depression may peak in spring, (1) summer, and winter months (11). Rihmer (11) demonstrated two different peaks depending upon bipolar subtype. Those with bipolar I depression were mainly hospitalized in summer and winter, whereas for bipolar II depression most admissions for depression occurred in the spring and summer. These results are similar to ours when we examined start date of major/minor depressive episodes, as bipolar I depression showed a peak in early and late summer; however, bipolar II depression exhibited a peak in autumn, specifically October and November. It is important to note that seasonal variation accounts for less variability in symptom burden than bipolar subtype. Our patient population is similar, but not an exact comparison, to previous studies and our data comes from a prospective cohort study, whereas prior studies retrospectively examined hospital admission statistics.

There are several limitations in our observational study, including the possibility of recall bias given that rating assessments for weekly symptomatic status were performed by interviews semiannually for the first five years of follow-up and annually thereafter. As a result, timing of polarity shifts could be misrepresented. Also, there is limited temporal resolution of one week given that data was only recorded in one-week intervals. In addition, these intervals do not correspond directly to *months*, therefore, there is potential for weeks to overlap with months, given that all weeks were determined retrospectively at six to 12 month intervals, which may lead to potential misclassification of symptom status by month. As mentioned previously, the ARIMA models were based upon indicators that were developed after descriptive statistics had already been performed.

Our study cannot account for local climate affecting seasonality, though all five academic centers fell within 38.75–42.37 degrees of latitude. We did not track location of individuals and there was no measurement of temperature and light exposure, which may affect circadian rhythms and contribute to seasonality (27). Also, our analysis focuses on aggregate

data by diagnosis and may miss individual seasonal patterns. In addition, treatment was not controlled for in this cohort and individuals received a variety of somatic therapies during follow-up, which could impact the intensity of mood symptoms. However, our sensitivity analysis suggests a pattern of seasonality in the largely untreated portion of our sample that is very similar to that in the treated portion.

The strengths of this study include the thorough assessments as well as the duration and intensity of follow-up that increased the accuracy of assessments. Our study is the largest and longest study using prospective data to assess seasonality in a cohort of individuals with bipolar disorder. We have no knowledge of a prospective study examining seasonality with a minimum follow-up of 10 years. Almost all prior studies examined admission data that does not capture much of what is experienced over the course of illness in mood disorders. Also, the intake diagnosis was given after an initial structured interview, as well as a comprehensive medical record review was performed, therefore decreasing the possibility of diagnostic misclassification.

In this long-term prospective cohort study, we confirm the presence of seasonal variation in bipolar disorder and identify a particular trend for peaks in manic/hypomanic symptomatology around the fall solstice, followed by peaks in depressive symptomatology circa the winter equinox in bipolar I disorder. This pattern may be consistent with suggested links between hibernation and changes in sleep, energy, and behavior (28). Clinicians should heed these higher risk periods and identify seasonal patterns within individual patients to target appropriate treatment. Future study may be useful to identify individual patterns or subgroups with more prominent seasonal variation and any genetic determinants or clinical correlates thereof.

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Chief as the Co-Chairperson and Robert Hirschfeld, M.D. as the Program Coordinator. Other past contributors include: J. Croughan, M.D., M.T. Shea, Ph.D., R. Gibbons, Ph.D., M.A. Young, Ph.D., and D.C. Clark, Ph.D.

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Fig. 1.

Percent of weeks with clinically significant depressive symptoms by month and bipolar subtype. Individuals with bipolar II disorder displayed a greater percentage of weeks with depression than did participants with bipolar I disorder. Seasonal variation is not prominent but more depressive morbidity is endured in the winter months and less in the summer months.

Fig. 2.

Percent of weeks with clinically significant manic/hypomanic symptoms by month and bipolar subtype. Participants with bipolar I disorder displayed a greater percentage of weeks with mania than did individuals with bipolar II disorder. Individuals with bipolar disorder, particularly bipolar II disorder, demonstrated a peak in hypomanic symptomatology in the months surrounding the autumnal equinox.

Fig. 3.

Timing of relapse with depressive episodes by bipolar subtype. There were a total of 772 and 693 new episodes of major depression in bipolar I and bipolar II, respectively. New onset depressive episodes were more common in May and August for bipolar I disorder and October and November for bipolar II disorder.

Fig. 4.

Timing of relapse into manic/hypomanic/mixed episodes by bipolar subtype. There were a total of 502 and 83 new episodes of mania/hypomania in bipolar I and bipolar II, respectively. Hypomanic episodes in bipolar II disorder were more commonly observed in August (15.7% of all new episodes).

Table 1

Sociodemographic and clinical characteristics of the sample by bipolar subtype at study entry

Characteristics	Bipolar I disorder (n = 202)	Bipolar II disorder (n = 112)	Entire sample (n = 314)
Sex, n (%)			
Male	80 (40)	31 (28)	111 (35)
Female	122 (60)	81 (72)	203 (65)
Inpatient, n (%)	176 (87)	72 (64)	248 (79)
Marital status, n (%)			
Married/partnered	83 (41)	46 (41)	129 (41)
Divorced/separated	33 (16)	21 (19)	54 (17)
Single	73 (36)	41 (37)	114 (36)
Widowed	13 (6)	4 (4)	17 (5)
Education, n (%)			
Without diploma	34 (17)	22 (20)	56 (18)
Highschool graduate	58 (29)	27 (24)	85 (27)
Some college	48 (24)	39 (35)	87 (28)
College graduate	62 (31)	24 (21)	86 (27)
Age at study intake, years			
Mean (SD)	35.3 (11.3)	34.3 (11.8)	34.9 (11.5)
Median (IQR)	34 (42–27)	31 (41–25)	33 (42–26)
Age at onset of first lifetime affective episode, years			
Mean (SD)	27.5 (13.8)	24.7 (12.5)	26.5 (13.4)
Median (IQR)	23 (35–18)	21 (28–17)	22 (33–18)

SD = standard deviation; IQR = interquartile range.

Table 2

Psychiatric Status Scale for episodic affective disorders

Code	Term	Definition
6	Definite criteria severe	Meets RDC criteria for definite and either prominent psychotic symptoms or extreme impairment in functioning
5	Definite criteria	Meets RDC criteria for definite but no prominent psychotic symptoms and no extreme impairment in functioning
4	Marked	Does not meet definite RDC criteria but has major symptoms or impairment from this disorder
3	Partial remission	No more than moderate impairment in functioning, but still has obvious evidence of the disorder
2	Residual	Either patient claims not to be completely back to <i>usual self</i> or rater notes the presence of one or more symptoms of this disorder in no more than a mild degree
1	Usual self	Patient returns to <i>usual self</i> without any residual symptoms of this disorder

This table represents the scale that raters used during follow-up to quantify symptom severity for major depression and mania. Clinically significant symptomatology was based on a rating of ≥ 3 . RDC = Research Diagnostic Criteria.

Table 3

Psychiatric Status Scale for all other conditions (chronic minor and intermittent depression, hypomania)

Code	Term	Definition
3	Definite criteria severe	Meets definite RDC criteria for this disorder
2	Probable criteria mild	Previously met RDC criteria for chronic minor/intermittent depression, minor depression, intermittent depressive features, or hypomania and now has some minor manifestations of one of these disorders
1	Not present	Previously met RDC criteria for the disorder but currently there is no evidence of this disorder

This table represents the scale that raters used to quantify symptom severity for minor and intermittent depression or hypomania. Clinically significant symptomatology was based on a rating = 3 on these scales. RDC = Research Diagnostic Criteria.