

## Seasonal changes, sleep length and circadian preference among twins with bipolar disorder

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## Abstract

**Background:** We aimed at studying the seasonal variation in mood, behaviour and hospital admissions, the effects of local weather conditions on wellbeing, and the morningness-eveningness preference and the persistence of the circadian type in twins with bipolar disorder and their healthy co-twins.

**Methods:** All Finnish like-sex twins born from 1940 to 1957 were screened for a diagnosis of bipolar type I disorder. The diagnosis was assessed with a structured research interview, and the study subjects (n=67) filled in the Seasonal Pattern Assessment Questionnaire (SPAQ). The Horne-Östberg morningness-eveningness questionnaire the study subjects filled in 2002. To study the persistence of the circadian type and sleep length, we used information collected with the Finnish Twin Cohort Questionnaire. Bipolar twins were compared with their healthy co-twins.

**Results:** Bipolar twins had greater seasonal changes in sleep length ( $p=0.01$ ) and mood ( $p=0.01$ ), and a higher global seasonality score ( $p=0.03$ ) as compared with their co-twins with no mental disorder. Sunny days ( $p=0.03$ ) had a greater positive effect on wellbeing in the bipolar than healthy co-twins.

**Conclusions:** Our results support the view that there is marked seasonal variation in bipolar disorder. Exposure to natural light appears to have a substantial effect on wellbeing in twins with bipolar disorder.

**Limitations:** The extent of changes in mood and behaviour and those in wellbeing was assessed retrospectively using a self-rating scale.

**Keywords:** Bipolar disorder; Mood; Season; Twin; Weather; Circadian type; Morningness Eveningness

## Background

Approximately 10% of all affective disorders show a seasonal pattern of recurrence, half of these being recurrent depressive disorders and the other half bipolar disorders [1]. Studies that have considered the onset of depressive episodes usually report two peaks of incidence: one in spring, and another in autumn [2]. In patients with bipolar disorder, admissions for manic and depressive episodes frequently follow a seasonal pattern with peaks in either autumn or winter, or autumn and spring [3, 4]. However, lack of seasonal variation in admissions due to bipolar disorder has also been reported [5].

Patients suffering from seasonal changes in mood and behaviour are frequently recognized as having affective disorder but other primary diagnoses are also common [6]. In particular, seasonal affective disorder is a form of recurrent major depressive or bipolar disorder with a seasonal pattern for which light therapy has been established as the first-line treatment option [7, 8]. It usually takes the course with winter depressive episodes plus summer remissions, although in some cases the pattern may be reversed [9].

Recently, it has been noticed that not only depressed but also bipolar patients staying in sunny hospital rooms seem to recover more rapidly than those in dull rooms [10, 11]. Low levels of illumination appear to be linked to the emergence of atypical depressive symptoms even among healthy people [12]. To sum up, there is marked seasonal variation in affective disorders, and they seem to be responsive to a number of environmental stimuli, such as exposure to light.

Disruptions in the sleep-wake cycle can be a trigger of manic episodes in bipolar disorder [13]. There may also be substantial changes in sleep length by season. In addition, twin studies suggest that there is genetic susceptibility to seasonal changes [14, 15]. It seems likely that patients with bipolar disorder have greater seasonal changes in mood and behaviour and those in sleep length than subjects with no mental disorder.

Morningness or eveningness, an endogenous component of the circadian clock, is characterized by inter-individual differences in circadian phase and requires a specific timing of complex behaviours. A subjective report of preferences for morning or evening activities is predictive of individual preferred bedtimes, and there is a strong link between the preferred sleep patterns and peak body temperature times indicative of the intrinsic period [16-19]. Depressed patients have more frequently eveningness preference as compared with healthy individuals [20], but there are no such data concerning bipolar disorder.

### Study aims

We aimed at studying the seasonal variation in hospital admissions and self-reports of wellbeing in twins with bipolar disorder. We predicted that twins with bipolar disorder would present more pronounced changes in the latter than their healthy co-twins. We also aimed at assessing the circadian preferences, sleep length and seasonal patterns in mood and behaviour among twins with bipolar disorder.

## Methods

### Subjects

We started the search for study participants with the National Hospital Discharge Register of Finland to identify all patients with at least one of the following ICD-8 codes 296.10 or 296.30 in 1969–86 [21], or DSM-III-R codes 296.4, 296.5 or 296.6 in 1987–91 [22]. Dates for each episode were recorded. The National Population Register was thereafter used to locate twins born between 1940 and 1969. We also checked up the Finnish Twin Cohorts to identify any additional twins [23]. One twin pair with no history of mental illness was included to increase the number of healthy controls. The pair was related to a treating person contacted during the bipolar study. All the twins identified were sent an invitation to participate with their co-twin in the study. 67 twins filled the Seasonal Pattern Assessment Questionnaire (SPAQ) as part of the research interviews which took place during November 1998 to December 1999. Six twins refused any further contacts, and, finally, 61 twins were sent the Morningness-Eveningness Questionnaire (MEQ) in January 2002. The response rate was 62% (36 out of 61).

### Diagnostic assessment

All the probands and co-twins were interviewed by one of the authors using the structured clinical interview for DSM-IV diagnoses [24]. Interviews were made blind to zygosity. The diagnostic procedure has been described in detail elsewhere [25]. The zygosity determination was based on genetic marker analysis, and on questionnaires on resemblance during childhood [26].

## Assessment of seasonal changes and circadian type

The SPAQ was used for the assessment of seasonal variation in the length of sleep, social activity, mood, weight, appetite, and energy level [7]. The sum of these six scales yields the Global Seasonality Score (GSS), which can range from 0 to 24. This questionnaire also investigated the changes in wellbeing caused by local weather conditions. The sum of these ten scales yields a global score, designated here as the Global Weather Score (GWS), which can range from -30 to +30. Negative scores indicate negative effects and positive scores indicate positive effects of changes in weather conditions on feelings of wellbeing. In addition, two new variables were made from the SPAQ, and coded and analysed separately: light exposure (the sum of sunny days, and long days) and grey, cloudy days (the sum of grey cloudy days, foggy smoggy days, and short days).

The MEQ is a self-report questionnaire that has been used for the assessment of preferred timing of behaviour [27]. The questionnaire includes 19 questions, and the sum yields the Morningness-Eveningness Score (MES), which can range from 16 to 86. The highest scores indicate definite morningness, and the lowest ones definite eveningness. The FTCQ included one question concerning the circadian type (question #19 of the MEQ).

## Sleep length

To study the sleep length and subjective feeling of sleep debt, we used data that were available with the Finnish Twin Cohort Questionnaire (FTCQ) in 1975, 1981 and 1990. The overall response rate was 89% in the 1975 survey, 84% in 1981 and 77% in 1990. The FTCQ also included two questions about sleep length ("How many hours you usually sleep at night?", and "How many hours

you estimate to need to sleep, to feel perky next day?"). A new variable, sleep debt, was calculated from two questions by subtraction.

## Statistics

To take into account the correlated nature of twin data, we used adjusted Pearson F-statistics and Wald tests for clustered data to compare bipolar with healthy twins [28]. This method caters for the fact that there were pairs in which both twins had bipolar disorder. Survey estimation prevalences were applied for assessment of the domain and sum variables of the data derived from the questionnaires [29]. The Wilcoxon signed ranks tests were computed for the analysis of differences in these scores within the discordant twin pairs, i.e. in which one twin had bipolar disorder and the other did not. Intrapair correlations were calculated for the GSS and GWS, and partial correlation coefficients to estimate the association between the MES and the GSS. Chi-square and Fisher's exact tests were used for analysis of differences in categorical variables.

## Ethics

The Ministry of Social Affairs and Health, and the Ethics Committee of the National Public Health Institute approved the study. Written informed consent was obtained from all subjects after they received a complete description of the study.

## Results

The sample consisted of 67 study subjects (Table 1). Of them, 39 had bipolar disorder with the mean age of 44.3 years (ranging from 29 to 57), and 20 were assessed as healthy (no mental disorder) with the mean age of 44.7 years (ranging from 33 to 57). In addition, 8 had mental disorder other than bipolar disorder, and they were excluded from further analysis.

There was a greater proportion of men among the bipolar than healthy twins ( $F[1, 37]=4.75$ ,  $p=0.04$ ), but no difference in the affection status by zygosity. The number of discordant pairs was 15.

### Seasonal variation in hospital admission

Twins with bipolar disorder had most (31 %) of their hospital admissions during autumn (Table 2). The distribution of depressive and manic episodes did not differ significantly by season ( $\chi^2=7.36$ ,  $df=3$ ,  $p=0.06$ ), although the depressive episodes were most common in autumn and winter, and manic episodes in autumn and summer. We also counted the most frequent season of admission for each individual, with recurrent episodes ( $n=33$ ). Most of the admissions (52 %) occurred in the autumn, admission due to depressive episodes being most frequent during autumn and winter (82 %), and admissions occurred due to manic episodes during autumn, spring, or summer (83 %). We compared seasonal distribution of hospital admissions with the self-report of feeling of worst, as assessed with the SPAQ ( $\chi^2=2.29$ ,  $df=1$ ,  $p=0.13$ ). Similarly, we analysed the self-report length of sleep. The period of sleeping most did coincide with the admissions, were as period of sleeping least did not.

### Seasonal changes in mood and behaviour

There were significant differences in the extent of seasonal changes in mood ( $F[1, 36]=6.24$ ,  $p=0.02$ ), weight ( $F[1, 37]=5.88$ ,  $p=0.02$ ), appetite ( $F[1, 37]=4.76$ ,  $p=0.04$ ), and levels of energy ( $F[1, 37]=5.98$ ,  $p=0.02$ ), as well as in the GSS ( $F[1, 37]=9.73$ ,  $p=0.004$ ) between the bipolar and healthy twins. The changes were of greater extent in the bipolar twins.

### Weather associated changes in wellbeing

There was a significant difference in the effect of dry days on feelings of wellbeing ( $F[1, 34]=4.34$ ,  $p=0.04$ ) between the bipolar and healthy twins. Dry days induced a more positive effect on wellbeing in the bipolar twins. Interestingly, short days had only a negative effect on wellbeing in the monozygotic twins, whereas the response was diverse among the dizygotic twins ( $\chi^2=7.92$ ,  $df=2$ ,  $p=0.02$ ).

### Analysis of discordant pairs

There were greater seasonal changes in sleep length ( $Z=-2.58$ ,  $p=0.01$ ), and mood ( $Z=-2.50$ ,  $p=0.01$ ), and the GSS ( $Z=-2.23$ ,  $p=0.03$ ) was higher in the bipolar twins compared with their healthy co-twins. In addition, sunny days ( $Z=-2.15$ ,  $p=0.03$ ) had a greater positive effect on wellbeing in the bipolar than healthy co-twins. The mean difference (95 % CI) between the bipolar and healthy twins in the GSS was 3.40 (0.65 to 6.15), in sleep length 1.00 (0.36 to 1.64), in social activity 0.80 (0.01 to 1.59), in mood 0.93 (0.29 to 1.58), and in sunny days 1.00 (0.15 to 1.85).

### Analysis of intrapair correlations

The intrapair correlation of the GSS was 0.16 for seven monozygotic twin pairs ( $p=0.73$ ), and 0.21 for twenty dizygotic twins ( $p=0.38$ ). The intrapair correlation of the GWS was -0.16 for the monozygotic twins ( $p=0.76$ ), and 0.04 for the dizygotic twins ( $p=0.88$ ).

### Sleep length and debt

The bipolar twins slept longer nights, as self-reported with the FTCQ in 1990, compared with healthy twins ( $F[1, 18]=7.47$ ,  $p=0.01$ ; see Table 3). In follow-up 1999, as assessed in the interview, the mean sleep length was 8.21 hours in the morning types and 7.66 hours in the evening types, as calculated from the SPAQ. When we compared data on sleep length derived from the SPAQ with those from the FTCQ, healthy morning and evening types slept less in 1999 than 1981. The morning types with bipolar disorder slept more in 1999 than 1981. The evening types with bipolar disorder were equal with sleeping or less than before. The longest sleep length was 8.59 hours among the morning types (in winter), and the shortest one was 6.70 among the evening types (in summer).

### Circadian type

Among in the whole twin cohort, the stability of circadian preference remained good from 1981 to 1986 ( $\chi^2=134.4$ ,  $df=9$ ,  $p<0.0001$ ). The morning type tended to become slightly more prevalent with ageing in the whole cohort, as well as in our study sample (Figure 1). There were no significant differences in the MES ( $F[1, 24]=0.17$ ,  $p=0.68$ ), or the circadian type preferences ( $F[1, 25]=0.02$ ,

$p=0.88$ ) between the bipolar and healthy twins. We also checked whether the sum scores differed between monozygotic and dizygotic twins, or between men and women. We found no differences. The eveningness preferences was associated with a higher GSS (partial correlation,  $r = -0.045$ ,  $p < 0.01$ ) after controlling for sex, age, zygosity, and affection status. This association was seen only for the total score, and there were no significant associations between the circadian type and the seasonal changes in length of sleep, weight or appetite. Most often, the weight and appetite increased in winter and decreased in summer. The most common change in weight (in 51% of the individuals) was 2 to 3.5 kg during the year, and the food preferences changed in 32% of individuals by season.

## Discussion

The autumn was generally the worst time to patients with depressive and manic episodes, especially for those with recurrent episodes. The influence of autumn on mental wellbeing should be noticed with more care in clinical work. Surprisingly, the self-report of feeling worst did not match with the temporal distribution of depressed and manic episodes, instead the period of sleeping most indicating the depressive episode. Our results agree with previous reports in that increasing sleep associated with compromised wellbeing and increased mortality [30, 31].

Our main finding was that seasonal changes in sleep length and those in mood were greater in twins with bipolar disorder compared with their co-twins with no mental disorder. Interestingly, sunny days had a greater positive effect on wellbeing in the bipolar twins who in addition had a higher global seasonality score than their healthy co-twins. These findings support the view that bipolar disorder is associated with marked seasonal variation and the course of illness is susceptible to the perceived light exposure from the habitat. Recently has reported that light therapy enhanced the effects of total sleep deprivation on the perceived mood of bipolar depressed patients (24).

Our findings suggest that the subjectively-reported seasonality is related to phenotypic expression of bipolar disorder and not to underlying genetic susceptibility to seasonality as previous claimed. Our results did not agree with previous reports [14, 15] in that there is a marked genetic impact on the reporting of seasonal changes in mood and behaviour. However, our study population was small and not a representative one, but consisted of bipolar patients and their siblings. While high scores on the GSS are correlated with bipolar disorder, it may be that the genetic component cannot be detected in this kind of study sample. For the GWS, either, there was no evidence of genetic influence in this sample, but specific environmental factors had a significant effect on changes in wellbeing related to local weather conditions such as hours of sunshine. Therefore, our findings need to be considered as preliminary and interesting, but not of sound evidence or confirmative value.

In addition, eveningness has been associated with a greater need for sleep [32]. In our study, the evening types had more sleep debt than the morning types. This finding agrees with the previous data on that the evening types experience a need for longer sleep. During the follow-up from 1981 to 1999, the length of sleep shortened among the healthy twins. Shortage of sleep has been a common phenomenon in western societies. On the contrary, bipolar twins slept even more in 1999. These changes in circadian type preferences and the increasing need of sleep might reflect specific circadian vulnerability related to bipolar disorder, being different from that proposed for major depressive disorder.

### Limitations

Our study was a study of twins, which can limit the generalisation of the results. In addition, both the seasonal variation in mood and behaviour and the changes in wellbeing related to local weather conditions were retrospectively assessed using a self-rating scale. Scores on the SPAQ seem to vary

by season, but not by seasonal differences in the amount of daylight [33]. However, this is not a limitation in our study, because the SPAQ was administered with the research interviews that were distributed over the year. While depressed patients show eveningness preference compared with healthy individuals [6], bipolar patients were not more often of the evening type compared with their healthy co-twins. Our results support the view that bipolar disorder and major depressive disorder are distinct entities, and that they have differing pathophysiology related to the circadian systems. We also found that the eveningness was associated with a higher global seasonality score. It is therefore likely that the mechanisms affecting the phenotypes of circadian type and seasonality are the same, and shared or at least related to each other. For the assessment of circadian type, the sample size was relatively small, but derived from an extensive population-based sample using the National Population Register and the Finnish Twin Cohort. There is no previous report of the differences in the circadian type in patients with bipolar disorder. Our results of changes in circadian type preferences and increased sleep length during the follow-up in bipolar twins could be consequences of the illness itself, or of treatments used. Unfortunately, we were not able to evaluate these effects more profoundly.

## Conclusions

Our results support the view that there is marked seasonal variation in bipolar disorder. Exposure to natural light appears to have a substantial effect on wellbeing in twins with bipolar disorder. Changes in the circadian type were common in bipolar disorder, but the patients were not, however, more often the evening types, as supposed a priori.

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Figure 1. Morning and evening types (%) by age and sex (n of men=11404, n of women=12445)

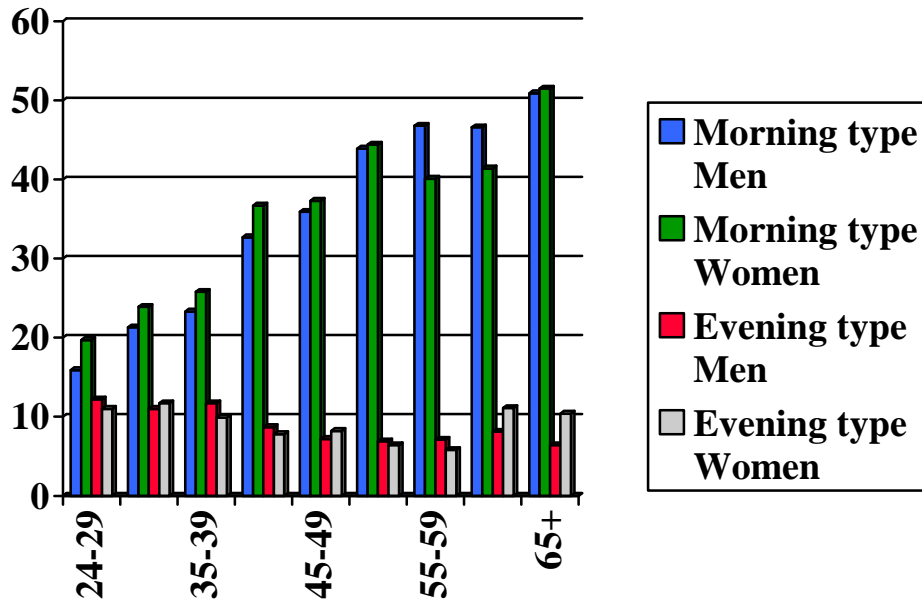


Table 1. The study sample of bipolar disorder twins and co-twins who have participated in the interview in 1998-1999 (n=67).

Diagnostic Status	Zygosity	Sex
Both twins participated, n= 54		
BP*-Healthy*	DZ	FF
BP*-Healthy*	DZ	FF
BP*-Healthy*	DZ	FF
BP*-Healthy*	DZ	MM
BP*-Healthy	DZ	MF
BP-Healthy*	DZ	MF
BP-Healthy*	DZ	FF
BP- Healthy*	DZ	FF
BP*-Healthy	DZ	FF
BP*-Healthy	MZ	FF
BP-Healthy*	DZ	FF
BP-Healthy*	DZ	FF
BP*-Healthy	DZ	FF
BP-Healthy	DZ	MM
BP-Healthy	MZ	MM
BP- Alcohol abuse	DZ	MM
BP-Alcohol abuse*	DZ	FF
BP*-MDD	DZ	FM
BP*-Schizophrenia*	MZ	MM
BP*-MDD*	DZ	FF
BP*-MDD*	DZ	FF
BP*-BP*	MZ	FF
BP*-BP*	DZ	FF
BP*-BP	MZ	MM
BP*-BP	DZ	MM
BP-BP	MZ	MM
Healthy-Healthy	MZ	FF
One twin participated n=13 (Co-twin did not participated, n=13)		
BP*-(Schizophrenia)	DZ	MM
BP*-(BP)	DZ	MM
BP*-(Healthy)	DZ	MM
BP-(Alcohol abuse)	DZ	MM
Healthy- (BP)	DZ	MM
Healthy-(BP)	DZ	MM
BP-(Healthy)	DZ	MM
Healthy-(BP)	DZ	MM
BP-(BP)	DZ	MM
MDD-(BP)	MZ	FF
Post partum depression-(BP)	DZ	FM
BP-(Schizophrenia)	DZ	FM
BP-(BP)	DZ	MM

\*Subjects who filled in the MEQ in 2002, n=36.

Abbreviations: BP= bipolar disorder, MDD= major depressive disorder  
DZ=dizygotic, MZ= monozygotic, M= male, F=female

Table 2. Seasonal variation in episodes in twins with bipolar disorder

Season	Episodes		
	depressive	manic	
Autumn	20	42	62
winter	13	29	42
spring	7	36	43
summer	8	46	54
	48	153	201

Table 3. Sleep length and debt, global score (GSS), global weather score (GWS), and Morningness-Eveningness Score (MES) by affection status.

	Bipolar disorder			No mental disorder		
	n	mean	95% CI	n	mean	95% CI
FTCQ						
sleep length (h)						
In 1975	21	7.86	7.61 to 8.11	9	7.83	7.56 to 8.11
In 1981	22	7.77	7.38 to 8.17	12	7.79	7.28 to 8.31
In 1990	18	7.92	7.48 to 8.35	10	7.15	6.81 to 7.49
sleep debt (h)						
In 1981	22	-0.34	-0.74 to 0.06	12	0.04	-0.24 to 0.33
In 1990	18	-0.25	-0.85 to 0.35	10	0	-0.24 to 0.24
SPAQ						
GSS	39	8.21	6.82 to 9.59	20	5.20	3.49 to 6.91
GWS	37	2.43	0.52 to 4.34	19	1.32	-0.05 to 2.68
MES	21	53.29	50.2 to 59.2	11	54.64	50.2 to 59.1

Abbreviations: FTCQ= The Finnish Twin Cohort Questionnaire, SPAQ= The Seasonal Pattern Assessment Questionnaire, MES= The Morningness-Eveningness Score