

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

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Abstract

Background: We aimed at studying the seasonal changes in mood and behaviour, the distribution of hospital admissions by season, 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 1969 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) and the Morningness-Eveningness Questionnaire (MEQ). For studying the persistence of the habitual sleep length and circadian type, we used data derived from the Finnish Twin Cohort Questionnaire (FTCQ). 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 higher global seasonality scores ($p=0.03$) as compared with their co-twins with no mental disorder. Sunny days ($p=0.03$) had a greater positive effect on well-being in the bipolar than healthy co-twins.

Conclusions: Our results support the view that bipolar disorder is sensitive to the environmental influence in general and to the seasonal effect in specific. Exposure to natural light appears to have a substantial effect on well-being in twins with bipolar disorder.

Limitations: Changes in mood and behaviour and those in well-being were assessed retrospectively using a self-ratings scale. Data have been collected from Finland, a country residing at far northern latitudes, which can limit the generalisation of our results.

Keywords: Bipolar disorder; Circadian type; Mood; Season; Twin; Weather

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 the peaks during either autumn or winter, or autumn and spring [3,4]. However, the 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 recognised as having an 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 that are followed by 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.

There may also be substantial changes in sleep length by season. Disruptions in the sleep-wake cycle can be a trigger for manic episodes in bipolar disorder [13]. Twin studies suggest that there is genetic susceptibility to seasonal changes [14,15]. Therefore, 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 characterised by inter-individual differences in circadian phase and requires a specific timing of complex behaviours. A subjective report of the preference for morning or evening activities is predictive of individually preferred bedtimes, and there is a strong link between the preferred sleep-wake schedules and peak body temperature times indicative of the intrinsic period [16-19]. Depressed patients have more frequently the preference of evening activities as compared with healthy individuals [20], but there are no such data concerning bipolar disorder.

Study aims

We aimed at studying these seasonal variations in hospital admissions and self-reports of well-being 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. Another aim was to study the effect of natural light exposure. We predicted that exposure to natural light would have positive effects on well-being in twins with bipolar disorder. We also aimed at assessing the circadian preference, sleep length and seasonal pattern 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 in order 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 the Finnish Twin Cohort to identify any additional twins [23]. One twin pair with no history of mental illness was included to increase the number of healthy controls. All the twins identified were sent an invitation to participate with their co-twin in the study. 67 twins filled in the Seasonal Pattern Assessment Questionnaire (SPAQ) as part of the research interviews that took place during the period of November 1998 to December 1999. Six twins refused from 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]. The 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 the questionnaire 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), ranging from 0 to 24. The SPAQ also investigated the experienced changes in wellbeing attributed to local weather conditions. The sum of these ten scales yields a global score, designated here as the Global Weather Score (GWS), ranging from -30 to +30. Negative scores indicate negative effects and positive scores indicate positive effects on wellbeing. In addition, two new variables were coded and thereafter analysed separately: bright light exposure

(the sum of sunny days plus long days) and dim light exposure (the sum of grey cloudy days plus foggy or smoggy days plus short days).

The MEQ is a self-report questionnaire that has been used for the assessment of preferred timing of complex behaviours [27]. The MEQ includes 19 items, and the sum yields a global score, designated here as the Morningness-Eveningness Score (MES), ranging from 16 to 86. The highest scores indicated definite morningness, and the lowest scores definite eveningness. The Finnish Twin Cohort Questionnaire (FTCQ) included one question concerning the circadian type (item #19 of the MEQ). We used the data on this item for studying the stability of circadian preference.

Sleep length

To study the sleep length and subjective feelings of sleep debt, we used the data derived from the FTCQ administered in 1975, 1981 and 1990. The overall response rates were 89%, 84% and 77%, respectively. The FTCQ 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 perk up next day?"). A new variable, sleep debt, was calculated from these 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 twin had bipolar disorder. Survey estimation prevalence was applied for the assessment of the domain and sum variables derived from the questionnaires [29]. The Wilcoxon signed rank 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.

Intra-pair correlations were recalculated 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 the analysis of categorical variables.

Ethics

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

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). The number of discordant pairs was 15. In addition, 8 subjects had mental disorder other than bipolar disorder, and they were excluded from subsequent analysis.

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

Seasonal variation in hospital admission

Twins with bipolar disorder ($n=39$) 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 the autumn and

winter, and manic episodes in the autumn and summer. We also counted the most frequent season of admission for each individual with recurrent episodes. Most of these admissions occurred during autumn (34% of all episodes, 33 patients), admissions due to depressive episodes being most frequent in the autumn and winter (67% of all episodes, 11 patients) and admissions due to manic episodes in the autumn, spring, or summer (86% of all episodes, 29 patients).

This seasonal distribution of hospital admissions did not match with the self-reports of feeling worst, as assessed with the SPAQ ($\chi^2=2.29, df=1, p=0.13$). Similarly, we analysed the self-reported length of sleep. The period of sleeping most did coincide with the admissions, whereas the period of sleeping least did not.

Seasonal changes in mood and behaviour

There were significant differences in the extent of seasonal changes in mood (mean = 1.66, 95% CI of 1.35 to 1.97, and mean = 1.10, 95% CI = 0.73 to 1.47; $F[1, 36]=6.24, p=0.02$), weight (mean = 0.97, 95% CI of 0.65 to 1.29, and mean = 0.45, 95% CI of 0.13 to 0.77; $F[1, 37]=5.88, p=0.02$), appetite (mean = 0.90, 95% CI of 0.57 to 1.23, and mean = 0.40, 95% CI of 0.08 to 0.72; $F[1, 37]=4.76, p=0.04$), and level of energy (mean = 1.64, 95% CI of 1.27 to 2.01, and mean = 1.10, 95% CI of 0.73 to 1.47; $F[1, 37]=5.98, p=0.02$), as well as in the GSS (mean = 8.21, 95% CI of 6.82 to 9.59, and mean = 5.20, 95% CI of 3.49 to 6.91; $F[1, 37]=9.73, p=0.004$) between the bipolar and healthy twins, respectively. The changes were of greater extent in the bipolar twins.

Weather associated changes in well-being

There was a significant difference in the effect of dry days on feelings of well-being (mean = 1.47, 95% CI of 0.97 to 1.97, and mean = 0.68, 95% CI of 0.20 to 1.17; $F[1, 34]=4.34, p=0.04$) between

the bipolar and healthy twins, respectively. Dry days induced a more positive effect on wellbeing in the bipolar twins (in 23 of 30, 77%). 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 (mean=1.86, 95% CI of 1.22 to 2.49, and mean=1.07, 95% CI=0.46 to 1.68; $Z=-2.58, p=0.01$), and mood (mean=2.00, 95% CI of 1.45 to 2.55, and mean=1.07, 95% CI of 0.62 to 1.51; $Z=-2.50, p=0.01$), and the GSS (mean=8.73, 95% CI=6.41 to 11.06, and mean=5.33, 95% CI of 3.09 to 7.57; $Z=-2.23, p=0.03$) in the bipolar twins compared with their healthy co-twins, respectively. 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 intra-pair correlations

The intra-pair correlation of the GSS was 0.16 for these seven monozygotic twin pairs ($p=0.73$), and 0.21 for the twenty dizygotic twin pairs ($p=0.38$). The intra-pair 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, as assessed with the FTCQ in 1990, compared with healthy twins ($F[1,18]=7.47, p=0.01$; see Table 3). At follow-up, the mean sleep length was 8.21 hours for the morning types and 7.66 hours for the evening types, as assessed with the SPAQ in 1999. When we compared data on sleep length derived from the SPAQ with those from the FTCQ, healthy twins slept less in 1999 than in 1981 (Table 4). The morning types with bipolar disorders slept more in 1999 than in 1981. 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 the whole twin cohort (assessed with the FTCQ), the stability of circadian preference remained good from 1981 to 1986 ($\chi^2=134.4, df=9, p<0.0001$). Preference for morning activities tended to become slightly more prevalent with ageing in the whole cohort of 11,404 men and 12,445 women (Figure 1), as in our study sample. 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 (Table 3). The MES did not differ between monozygotic and dizygotic twins, or between men and women.

Preference for evening activities was associated with a higher GSS ($r=-0.045, p<0.01$), 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 changes in weight as well as those in appetite were reported to be greater in the winter and smaller in the summer. The most frequent

change in weight (in 51% of the individuals) was a gain of 2 to 3.5 kg during the year, and in 32% of the individuals there was a change in appetite by season.

Discussion

The autumn was generally the worst time for patients with depressive and manic episodes, especially for those with recurrent episodes. Therefore, the negative influence of autumn on mental wellbeing needs to be noticed with more care in clinical work. Surprisingly, these self-reports of feeling worst did not match with the temporal distribution of depressed and manic episodes, instead the period of sleeping most appeared to coincide with admissions due to a depressive episode. Our results agree with previous reports in that the increased length of sleep was indeed associated with compromised wellbeing [30,31].

Our main finding was that these 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, whom 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, it has also been shown that light therapy is likely to add on the efficacy of total sleep deprivation for the treatment of depressed patients with bipolar disorder [29].

Our findings suggest that the subjectively reported seasonal changes are related rather to the phenotype of bipolar disorder than to the genetic susceptibility to seasonal variation. Here, our results did not agree with previous reports [14,15] in that there would be a marked genetic impact on these seasonal changes in mood and behaviour. Our study population was small, but however 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 well-being 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.

Recently, the sex difference in circadian preference has been reported [32,33]. In our study, there was no such difference. In addition, preference for evening activities has been associated with a greater need for sleep [34]. In our study, the evening types had a greater sleep debt than the morning types. This finding agrees with the previous data showing that the evening types do experience a need for longer sleep. During the follow-up of 1981 to 1999, the length of sleep shortened among the healthy twins. The shortage of sleep has been a common phenomenon in western societies. In contrast, bipolar twins of four samples slept even more in 1999.

These changes in circadian type preferences and the increasing need for sleep might reflect specific factors underlying the circadian vulnerability in bipolar disorder, being different from the one proposed for major depressive disorder. The dual vulnerability hypothesis claims that an affective disorder with these seasonal patterns is a combination of a seasonal factor and a depression factor and consequently represents the extreme end of one trait. Subjects with a stronger seasonal factor primarily have vegetative symptoms (e.g. hypersomnia), without marked cognitive symptoms. At the opposite end of the trait, subjects with a stronger depression factor tend to have cognitive symptoms (e.g. insomnia), without marked vegetative symptoms [13,35]. Previous studies have reported that individuals with insomnia are more likely to have a major depressive disorder, and longitudinal studies have in addition shown that the persistence of insomnia tends to be associated with the appearance of a new depressive episode [33].

Limitations

Our study was a study of twins, which has such a limit to the generalisation of our results. Both the seasonal variation in mood and behaviour and the changes in well-being attributed to local weather conditions were retrospectively assessed using a self-reporting scale. Scores on the SPAQ tend to vary by season, but not by day length [36]. However, this is not a true limitation in our study, because the SPAQ was administered with the research interviews that were distributed evenly over the year. While depressed patients tend to show a greater preference for evening activities as compared with healthy individuals [6], our bipolar patients were not more often of the evening type than their healthy co-twins. We also found that the eveningness was associated with a higher global seasonality score. It is therefore likely that the mechanisms of action that affect the phenotypes of circadian type and those of the seasonal pattern are shared, or at least closely related to each other. For the assessment of circadian type, the sample size was small, but derived from an extensive population-based sample using the National Population Register and the Finnish Twin Cohort. The sample has been collected from Finland, a country residing at far northern latitudes, which can limit the generalisation of our results as far as the globe is concerned.

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 seasonal variation in bipolar disorder and the exposure to natural light appears to have a substantial effect on well-being. Patients with bipolar disorder were not more often the evening types.

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References

1. Faedda G L, Tondo L, Teicher MH, Baldessarini RJ, Gelbard HA, Floris GF: **Seasonal mood disorders. Patterns of seasonal recurrence in mania and depression** .*Arch Gen Psychiatry* 1993, **50**:17-23.
2. Fossey E, Shapiro CM: **Seasonality in psychiatry -- a review** .*Can J Psychiatry* 1992, **37**:299-308.
3. Parker G, Walter S: **Seasonal variation in depressive disorders and suicidal deaths in New South Wales** .*Br J Psychiatry* 1982, **140** :626-632.
4. Silverstone T, Romans S, Hunt N, McPherson H: **Is there a seasonal pattern of relapse in bipolar affective disorders? A dual northern and southern hemisphere cohort study** .*Br J Psychiatry* 1995, **167** :58-60.
5. Partonen T, Lonnqvist J: **Seasonal variation in bipolar disorder** .*Br J Psychiatry* 1996, **169** :641-646.
6. Partonen T, Piironen P, Lonnqvist J : **Season-dependent symptoms in consultant - liaison patients** .*International journal of psychiatry in clinical practise* 2000, **4** :151-154.
7. Rosenthal NE, Sack DA, Gillin JC, Lewy AJ, Goodwin FK, Davenport Y, Mueller PS, Newsome DA, Wehr TA: **Seasonal affective disorder. A description of the syndrome and preliminary findings with light therapy** .*Arch Gen Psychiatry* 1984, **41**:72-80.
8. Partonen T, Lonnqvist J: **Seasonal affective disorder** .*Lancet* 1998, **352**:1369-1374.
9. Wehr TA, Sack DA, Rosenthal NE: **Seasonal affective disorder with summer depression and winter hypomania** .*Am J Psychiatry* 1987, **144** :1602-1603.

10. BeaucheminKM,HaysP: **Sunnyhospitalroomsexpediter recoveryfromsevere andrefractorydepressions** *.JAffectDisord* 1996,**40** :49-51.
11. BenedettiF,ColomboC,BarbiniB,CamporiE,SmeraldiE: **Morningsunlight reduceslengthofhospitalizationinbipolardepression** *.JAffectDisord* 2001, **62**:221-223.
12. EspirituRC,KripkeDF,Ancoli-IsraelS,MowenMA,MasonWJ,FellRL,Klauber MR,KaplanOJ: **LowilluminationexperiencedbySanDiegoadults:association withatypicaldepressivesymptoms** *.BiolPsychiatry* 1994,**35** :403-407.
13. WehrTA,SackDA,RosenthalNE: **Sleepreductionasafinalcommonpathwayin thegenesisofmania** *.AmJPsychiatry* 1987,**144** :201-204.
14. MaddenPA,HeathAC,RosenthalNE,MartinNG: **Seasonalchangesinmoodand behavior.The roleofgeneticfactors** *.ArchGenPsychiatry* 1996,**53** :47-55.
15. JangKL,LamRW,LivesleyWJ,VernonPA: **Genderdifferencesintheheritability ofseasonalmood change** *.PsychiatryRes* 1997,**70** :145-154.
16. ÖstbergO: **Circadianrhythmsoffoodintakeandoraltemperaturein"morning" and"evening"groupsofindividuals** *.Ergonomics* 1973,**16** :203-209.
17. IshiharaK,MiyasitaA,InugamiM,FukudaK,MiyataY: **Differencesinsleep-wake habitsandEEGsleepparametersbetweenactivemorningandeveningsubjects** *. Sleep* 1987, **10**:330-342.
18. KerkhofGA, VanDongenHP: **Morning-typeandevening-typeindividualsdiffer inthephasepositionoftheirendogenouscircadianoscillator** *.NeurosciLett* 1996, **218**:153-156.
19. BaehrEK,RevelleW,EastmanCI: **Individualdifferencesinthe phaseand amplitudeofthehumancircadian temperature rhythm:withan emphasis on morningness-eveningness** *.JSleepRes* 2000, **9**:117-127.

20. DrennanMD, KlauberMR, KripkeDF, GoyetteLM: **Theeffectsofdepressionand ageontheHorne -Ostbergmorningness -eveningnessscore** .*AffectDisord* 1991, **23**:93-98.
21. OrganizationWH: *Manualoftheinternationalstatisticalclassificationofdiseases, injuries,andcausesofdeath* ,8thededn.Geneve:WorldHealthOrganization;1967.
22. AssociationAP: *DiagnosticandStatisticalManualofMentalDisorders* ,3rd,revised ededn.Washington,DC:AmericanPsychiatricPress;1987.
23. KaprioJ, KoskenvuoM, RoseRJ : **Population-basedtwinregistries:illustrative applicationsingeneticepidemiologyandbehavioralgeneticsfromtheFinnish TwinCohortStudy** .*ActaGenetMedGemellol* 1990,**39** :427-439.
24. SpitzerRL, GibbonM, WilliamsJBW: *ThestructuredClinicalInte rviewforDSM -IV AxisIandIIDisorders(SCIDIandII)* .Washington,DC:AmericanPsychiatricPress; 1997.
25. KieseppäT, PartonenT, KaprioJ, LönnqvistJ: **Accuraryofregister -andrecord - basedbipolarIdiagnosesinFinland -astudyoftwins** .*ActaNeuro psychiatrica* 2000,**12** :106-109.
26. SarnaS, KaprioJ, SistonenP, KoskenvuoM: **Diagnosisoftwinzygositybymailed questionnaire** .*HumHered* 1978,**28** :241-254.
27. HorneJ, ÖstbergO: **Aself -assessmentquestionnairetodeterminemorningness - eveningnessinh umancircadianrhythms** .*IntJChronobiol* 1975, **4**:97-110.
28. CorporationS: *STATAStatistics/DataAnalysis7.0.CollegeStation* :TX:STATA Corporation;2001.
29. ColomboC, LuccaA, BenedettiF, BarbiniB, CamporiE, SmeraldiE: **Totalsleep deprivationcombi nedwithlithiumandlighttherapyinthetreatmentofbipolar**

- depression: replication of main effects and interaction** *.Psychiatry Res* 2000, **95**:43-53.
30. Jean-Louis G, Kripke DF, Ancoli-Israel S: **Sleep and quality of well-being.** *Sleep* 2000, **23** :1115-1121.
31. Kripke DF, Garfinkel L, Wingard DL, Klauber MR, Marler MR: **Mortality associated with sleep duration and insomnia** *.Arch Gen Psychiatry* 2002, **59**:131-136.
32. Natale V, Adan A, Chotai J: **Further results on the association between morningness-eveningness preference and the season of birth in human adults** *. Neuropsychobiology* 2002, **46**:209-214.
33. Adan A, Natale V: **Gender differences in morningness-eveningness preference** *. Chronobiol Int* 2002, **19**:709-720.
34. Taillard J, Philip P, Bioulac B: **Morningness/eveningness and the need for sleep** *. J Sleep Res* 1999, **8** :291-295.
35. Lam RW, Tam EM, Yatham LN, Shiah IS, Zis AP: **Seasonal depression: the dual vulnerability hypothesis revisited** *. J Affect Disord* 2001, **63** :123-132.
36. Lund E, Hansen V: **Responses to the Seasonal Pattern Assessment Questionnaire in indifferent seasons** *. Am J Psychiatry* 2001, **158** :316-318.

Figure 1. Morning and evening types among the twin cohort.

Table 1. The study sample of bipolar disorder twins and co-twins.

Affection status	Zygoty	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

Onetwinparticipated,n=13(Co -twindidnotparticipate,n=13)

BP*-(Schizophrenia)	DZ	MM
BP*-(BP)	DZ	MM
BP*-(Healthy)	DZ	MM
BP-(Alcoholabuse)	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-partumdepression -(BP)	DZ	FM
BP-(Schizophrenia)	DZ	FM
BP-(BP)	DZ	MM

*SubjectswhofilledintheMEQin2002,n=36.Abbreviations:BP=bipolardisorder,MDD=major depressivedisorder,DZ=dizygotic,MZ=monozygotic, M=male,F=female.

Table 2. The seasonal pattern of episodes in twins with bipolar disorder.

Season	Episodes		total
	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, sleep debt, well-being and circadian preference by affection status.

	Bipolar disorder			Non-affective 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, GSS = Global Seasonality Score, GWS = Global Weather Score, MES =

Morningness-Eveningness Score.

Table 4. Sleep length in the morning and evening types by affection status.

Sleep length (h)	Bipolar disorder			Non-affective disorder		
	n	mean	95% CI	n	mean	95% CI
Morning type						
in 1981 from FTCQ	6	7.58	6.62 to 8.55	6	7.67	6.53 to 8.80
in 1999 from SPAQ	9	8.72	7.76 to 9.69	6	7.25	6.63 to 7.87
Evening type						
in 1981 from FTCQ	10	7.70	7.06 to 8.34	6	7.92	7.40 to 8.43
in 1999 from SPAQ	12	7.77	6.99 to 8.56	6	7.38	6.28 to 8.47

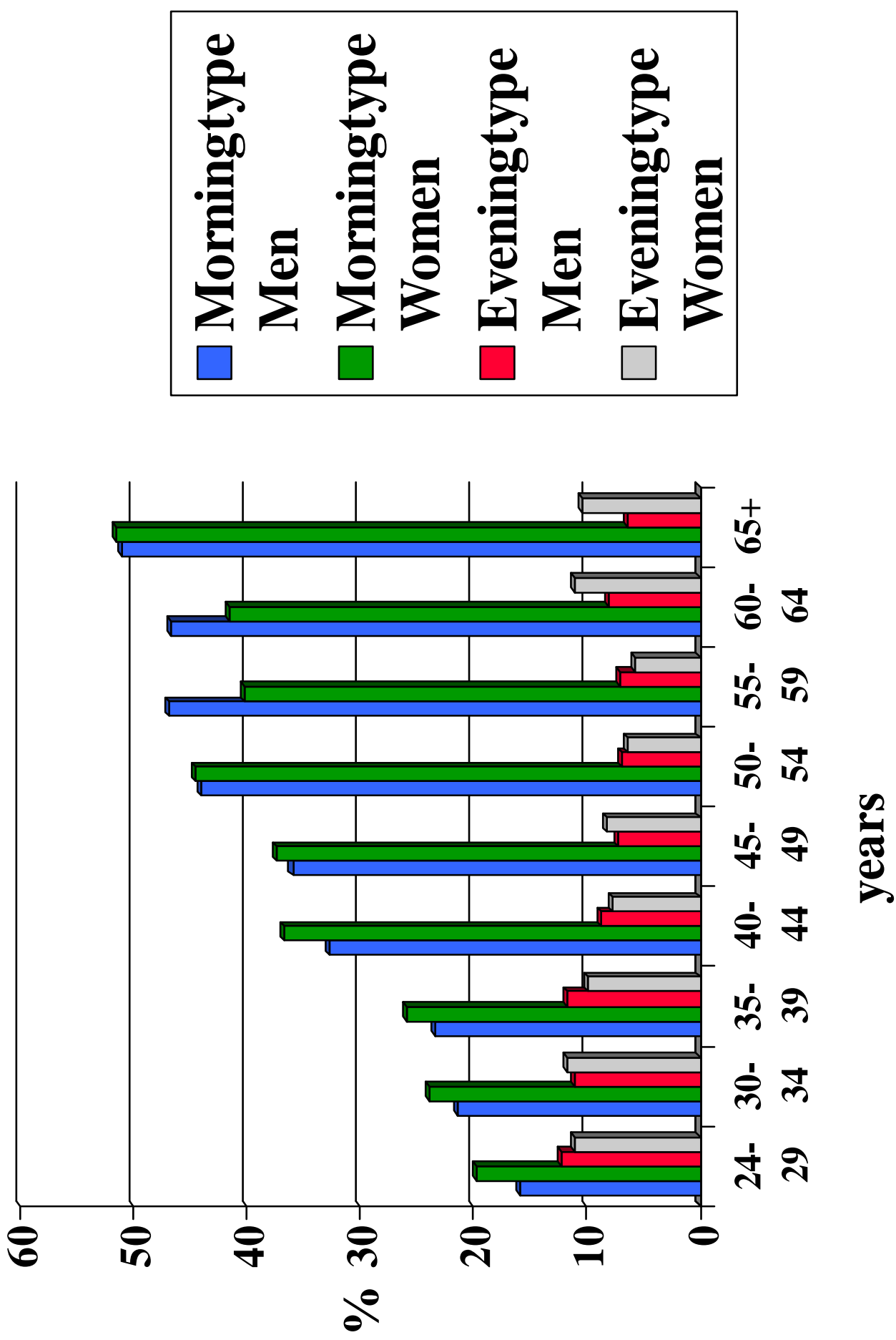


Figure 1