

Research report

Seasonal variations in bipolar disorder admissions and the association with climate: A population-based study

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Abstract

Objective: Although seasonal influences on bipolar disorder admissions have long been observed, the issues of seasonality on different subtypes of mood episodes and the effects of associated climatic parameters remain controversial. This study sets out to examine seasonal variations in bipolar disorder admissions and the association with climate in Taiwan, a subtropical area with fairly constant weather conditions.

Methods: This retrospective population-based study uses the Taiwan National Health Insurance Research Database for 1999–2003, identifying 15,060 admissions for bipolar disorder, comprising of 8631 manic, 2078 depressive and 4351 mixed/unspecified episodes. The auto-regressive integrated moving average model was applied to examine the presence of seasonality and the association with climate in each subtype of mood episodes.

Results: Admission peaks were noted during spring/summer, early winter and early spring, for manic, depressive and mixed/unspecified episodes, respectively, while the associations with climatic parameters varied between the subtypes of mood episodes.

Conclusions: Seasonality in bipolar disorder does exist for all subtypes of mood episodes. The distinct seasonal patterns and various associations with the climatic parameters imply different underlying mechanisms for the onset of each subtype of mood episodes. The association between admission rates and certain climatic variables found in this study is informative and could pave the way for future studies aimed at exploring the influence of climate on the psychopathology of bipolar patients as well as the underlying mechanisms.

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1. Introduction

As a result of their debilitating mood swings, most bipolar disorder patients will invariably experience re-

peated hospitalizations throughout their lifetime (Lish et al., 1994). The factors associated with bipolar disorder admissions have therefore been extensively investigated in an attempt to shed some light on prevention and early intervention for such distressing mood episodes. Given that seasonal variations in bipolar admissions have often been observed (Symonds and Williams, 1976; Hare and Walter, 1978; Myers and Davies, 1978; Frangos et al., 1980; Carney et al., 1988; Wehr and Rosenthal, 1989),

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seasonality and other related issues are clearly of interest in studies of patterns in bipolar disorder admissions.

Distinct seasonal influences have been reported on admission patterns between the different subtypes of mood episodes in bipolar disorder patients (Barbini et al., 1995; Whitney et al., 1999; Avasthi et al., 2001; Cassidy and Carroll, 2002; Morken et al., 2002). As regards manic episodes, the lines of evidence have largely suggested a spring/summer peak in related admissions (Symonds and Williams, 1976; Hare and Walter, 1978; Myers and Davies, 1978; Carney et al., 1988; Mulder et al., 1990; Sayer et al., 1991; Takei et al., 1992); however, the findings on seasonal influences in depressive episodes have been less consistent (Eastwood and Stiasny, 1978; Partonen and Lonnqvist, 1996; Morken et al., 2002; Shapira et al., 2004), although the notion of winter depression did become popular after the introduction of the concept of seasonal affective disorder (Rosenthal et al., 1984). As regards mixed episodes, very little attention has thus far been afforded to seasonal variations in admissions for such episodes, although a unique late summer peak has been suggested (Whitney et al., 1999; Cassidy and Carroll, 2002).

Despite the mechanisms underlying the seasonality of bipolar disorder remaining unclear, biological factors have generally been considered to be more relevant than other psychosocial correlates (Wirz-Justice and Richter, 1979; Wehr and Rosenthal, 1989; Clarke et al., 1999), with various climatic parameters including daily ambient temperature, relative humidity, atmospheric pressure, rainfall and hours of sunshine, having been found to contribute to seasonal variations in bipolar disorder admissions (Mawson and Smith, 1981; Abdul-Rahim et al., 1992; Lee et al., 2002; Salib and Sharp, 2002).

It is, however, rather difficult to undertake a comparison of the studies on seasonality in bipolar disorder; indeed, the earlier studies have tended to focus solely on either a single subtype of mood episodes, or have failed to delineate the distinct types of mood episodes in bipolar disorder (Eastwood and Stiasny, 1978; Parker and Walzter, 1982). Furthermore, ethnicity and geographical location have each been considered as potential confounders in the relationship between seasons and mood episodes (Suhail and Cochrane, 1997; Schaffer et al., 2003). Most of the prior studies have been conducted among Caucasian populations in temperate zones; however, while the studies undertaken in places other than the temperate zones of the northern and southern hemispheres remain extremely limited, they have in fact revealed quite different seasonal patterns in bipolar disorder (Jain et al., 1992; Kerr-Correa et al., 1998). The methodological limitations of these studies

have also resulted in findings which have been quite controversial and which have thus tended to compromise their generalizability.

Many of the prior studies have tended to use bipolar patient samples from elective hospitals, an approach which could clearly lead to selection bias due to the variations in practice styles between hospitals, such as the criteria for admissions and the number of available beds (Jain et al., 1992; Faedda et al., 1993; D'Mello et al., 1995; Silverstone et al., 1995; Kerr-Correa et al., 1998). The majority of the population-based studies have also made no attempt to explore the relationship between climatic parameters and bipolar disorder admissions (Walter, 1997; Jones et al., 1995; Clarke et al., 1998; Daniels et al., 2000). Furthermore, in many of these studies, of which very few were population-based, ordinary statistical methods, such as correlation or multiple regression analyses, have generally been selected as the means of testing the climate–admission relationship in bipolar disorder (Mawson and Smith, 1981; Sazlib and Sharp, 2002).

Reijneveld (1990) argued that certain modified statistical methods could prove to be better tests for seasonality, while more complex models may prove necessary for time series data. Carney et al. (1988), for example, found a significant correlation between mania admission rates and the total number of hours of sunshine, whereas Peck (1990) reported different findings in a reexamination of the same data under time series analysis.

Using a nationwide population-based database on Taiwan, this study sets out to examine seasonal variations in bipolar disorder admissions and to explore the association with climate. The database includes all claims data from Taiwan's National Health Insurance (NHI) program, a system which was implemented in March 1995 as a means of financing healthcare for all of the island's citizens. The NHI Bureau has contracted with all medical institutions providing psychiatric inpatient care in Taiwan, with around 96% of the island's population having joined the NHI program since its inception. Given its characteristics of a single-payer payment system, the NHI database offers a unique opportunity to investigate the issue of seasonality in bipolar disorder.

2. Methods

2.1. Hospitalization data

This study uses hospitalization data from the Taiwan National Health Insurance Research Database (NHIRD)

covering the years from 1999 to 2003; the database is published by the National Health Research Institute in Taipei. The NHIRD covers all inpatient and outpatient medical benefit claims for the Taiwanese population of over 23 million, and includes registries of contracted medical facilities, board-certified physicians, catastrophic illness patients, monthly claims summaries for inpatient claims and ambulatory care claims, details of inpatient orders and ambulatory care orders, and all expenditure on prescriptions dispensed at contracted pharmacies. The database provides one principal diagnostic code for each patient from the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9-CM).

2.2. Study sample

Between 1 January 1999 and 31 December 2003, there were a total of 64,718 hospital admissions for bipolar disorder involving 14,899 patients. These admissions were identified in the database by a principal diagnosis of episodes of single manic disorder (ICD-9-CM code 296.0), recurrent manic disorder (ICD-9-CM code 296.1), manic bipolar affective disorder (ICD-9-CM code 296.4), depressed bipolar affective disorder (ICD-9-CM code 296.5), mixed bipolar affective disorder (ICD-9-CM code 296.6), unspecified bipolar affective disorder (ICD-9-CM code 296.7), other and unspecified manic-depressive psychosis (ICD-9-CM code 296.8), and other and unspecified affective psychosis (ICD-9-CM code 296.9).

For many bipolar patients, a single episode will often involve more than one admission to hospital. Some suggest that mood episodes should be demarcated by partial or full remission for at least 8 weeks (American Psychiatric Association, 2002). Therefore, for those patients who had been readmitted within an 8 week period, only the first admission was recorded. Following the discarding of 49,658 readmissions, we were left with a study sample of 15,060 episodes, comprising of 8631 manic (ICD-9-CM codes 296.0, 296.1, and 296.4), 2078 depressive (ICD-9-CM codes 296.5), and 4351 mixed or unspecified episodes (ICD-9-CM codes 296.6, 296.7, 296.8, and 296.9). The mean age of the cohort was 40.4 years with a standard deviation of 14.9 years.

2.3. Population data

Population data in Taiwan are released annually to the public by the Population Affairs Administration at the Ministry of the Interior in Taiwan. The admission rate was defined in this study as the proportion (as a

fraction) of the total monthly admissions for the whole of the island's population in the same year. This study uses the data on population registrations in the Taiwan area to calculate the bipolar disorder admission rates per 100,000 of the population for the period 1999–2003.

2.4. Meteorological data

Meteorological data, comprising of daily ambient temperature, relative humidity, atmospheric pressure, rainfall, hours of sunshine, and maximum and minimum temperature, were obtained from 19 observation stations of the Central Weather Bureau (CWB) of Taiwan. Although the CWB has 26 observation stations spread out across the island, the meteorological data from seven stations was discarded, since these stations are located in the mountainous regions. The monthly mean values were then calculated by averaging the monthly data from the remaining 19 stations. Since Taiwan is a small island, with a total land mass slightly in excess of 36,188 km², we used only a monthly mean value for climatic data in order to explore the associations with bipolar disorder admission rates.

2.5. Seasons in Taiwan

Located between the northern latitudes of 21°45' and 25°56', Taiwan's weather is typically sub-tropical, and can be described as hot and humid all year round, with the demarcation between the seasons being quite vague. According to the seasonal definitions provided by the CWB, spring in Taiwan occurs from March to May, summer from June to August, autumn from September to November, and winter from December to February.

2.6. Statistical analysis

Monthly admission rates per 100,000 of the population for manic, depressive and mixed/unspecified episodes were calculated across the five-year study period, with seasonality being a general component of the time series pattern; the seasonality of the data was therefore evaluated by the 'auto-regressive integrated moving average' (ARIMA) regression method. This method, which describes a univariate time series as a function of its past values and other significant independent variables, has been used in many analogous studies as a means of testing for the presence of seasonality and the effects of environmental exposure. The ARIMA model uses autoregressive parameters, moving average parameters and the number of differencing passes to describe

Table 1
Monthly means of total, manic, depressive and mixed/unspecified admission rates, and climatic variables

Variable	Mean	S.D.	Minimum	Maximum
Total bipolar disorder*	1.12	0.15	0.58	1.62
Manic*	0.64	0.12	0.29	1.08
Depressive*	0.15	0.04	0.06	0.28
Mixed/unspecified*	0.32	0.05	0.18	0.44
Ambient temperature (°C)	23.1	4.1	16.2	29.3
Relative humidity (%)	77.9	2.9	70.3	82.6
Atmospheric pressure (hPa)	999.48	5.05	990.7	1007.9
Rainfall (mm)	159.3	40.1	63.2	283.2
Sunshine (h)	161.0	138.8	20.8	889.8
Maximum temperature (°C)	26.8	4.1	19.0	33.2
Minimum temperature (°C)	20.4	4.0	13.2	26.4

Note: * Total admissions per 100,000 population.

the series in which a pattern is repeated seasonally over time.

After controlling for time-trend effects, this study also adopted the ARIMA regression method as a means of evaluating the effects of climatic and monthly factors on bipolar disorder admission rates. The monthly factors included in the model were dummy variables, running from January to December, with a specific month being given a value of 1, while the remaining months were given a value of 0. Climatic factors included monthly mean ambient temperature, relative humidity, atmospheric pressure, rainfall, hours of sunshine, and maximum and minimum temperature.

The time trend was a count variable numbered from 1 to 60 according to the time series. Considering the parsimony of the models, only statistically significant independent variables were included in the ARIMA regression models.

The selection of the final model was based upon the lowest mean absolute percentage error, or mean absolute error, allowing the choice of the best model from the family of ARIMA regression models. All p values of <0.05 were considered statistically significant in this study.

3. Results

3.1. Admission rates

Throughout the period of this study, from 1999 to 2003, the total number of hospital admissions for bipolar disorder in Taiwan (excluding readmissions during the same episode) was 15,060. There were 3332 admissions in the year 1999, 3008 in the year 2000, 2939 in the year 2001, 2953 in the year 2002, and 2828 in the year 2003, with their respective admission rates (per 100,000 of the population) being 15.1, 13.5, 13.1, 13.10 and 12.5. Across the whole of the study period, the monthly bipolar disorder admission rates (per 100,000 of the population) ranged from a low of 0.58 in December 2003, to a high of 1.62 in January 1999, with a mean of 1.12 and a standard deviation of 0.15 (Table 1). The mean monthly admission rate for manic episodes was 0.64, while the respective mean rates for depressive and mixed/unspecified episodes were 0.15 and 0.32.

3.2. Seasonal variations

The seasonal variations in the admission rates for each separate subtype of bipolar disorder mood episodes, and for all of the subtypes pooled, are illustrated in Fig. 1, which indicates fairly similar seasonal patterns

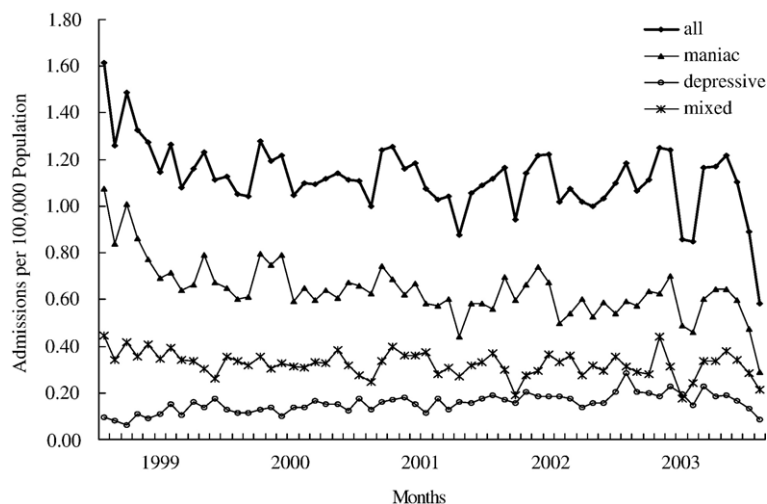


Fig. 1. Monthly admissions per 100,000 population of bipolar disorder from 1999 to 2003 in Taiwan.

in the admission rates for manic and combined episodes. The seasonal trends in admissions for manic episodes display a significant hospitalization trough in June (early summer), followed by a sharp increase in July, and a peak in August (late summer). Thereafter, there is a discernible downward trend beginning in September with a further trough being observed in November to December (late fall to early winter). The nadir in admissions for depressive episodes occurs in June and August (early and late summer). As to mixed/unspecified episodes, a trough is observed in February (late winter), which contrasts with a peak in March (early spring).

3.3. ARIMA regression model

The ARIMA test for seasonality was found to be significant for each subtype of mood episodes and for all of the subtypes pooled ($p < 0.001$ for all SAR); the results are presented in Table 2. The choice of model for the ARIMA test for manic episode admission rates was a

multiplicative model with respective trend and seasonality parameters of (1,0,0) and (4,0,0). The (1,0,0) (4,0,0) model indicates that there was one autoregressive parameter, no moving average parameters, four seasonal autoregressive parameters, and no seasonal moving average parameters. These parameters were computed for the series without any differencing (such as seasonal differencing). As compared to other months throughout the study period, the admission rates tended to be higher for March to May ($p < 0.001$) and July to August ($p < 0.001$), and lower for November ($p < 0.001$) and December ($p < 0.001$). The R^2 within the ARIMA model for admissions of manic episodes was as high as 0.754.

The choice of model for the ARIMA test for depressive and mixed/unspecified episode admission rates was a multiplicative model with respective trend and seasonality parameters of (1,0,0) (3,0,0) and (2,0,0) (4,0,0).

As regards the admission rates for depressive episodes, as compared to other months throughout the study period, the rates tended to be lower for May to

Table 2
ARIMA regression analysis of monthly admission rates for bipolar disorder

Independent variables	Monthly admission rates per 100,000 population								
	Manic episodes			Depressive episodes			Mixed/unspecified episodes		
	β	SE	<i>t</i> -value	β	SE	<i>t</i> -value	β	SE	<i>t</i> -value
Intercept	0.9067	0.0	37.91***	0.0211	0.01	1.44	0.3195	0.01	40.28***
AR1	0.2467	0.14	1.81	0.8239	0.08	9.76***	0.2378	0.09	2.64*
AR2	–	–	–	–	–	–	–0.2296	0.08	–2.79**
SAR1	–1.0807	0.26	–4.20***	–1.1372	0.11	–10.06***	–0.8814	0.11	–7.90***
SAR2	–1.1587	0.35	–3.31**	–0.9734	0.14	–6.88***	–1.2529	0.12	–10.53***
SAR3	–0.8990	0.30	–3.02**	–0.6885	0.11	–6.44***	–0.8150	0.12	–7.01***
SAR4	–0.5750	0.24	–2.38*	–	–	–	–0.7770	0.09	–9.09***
January	0.0190	0.01	2.01	–	–	–	–	–	–
February	–	–	–	–	–	–	–0.0218	0.00	–6.19***
March	0.0813	0.01	9.02***	–	–	–	0.0592	0.00	16.27***
April	0.0624	0.01	6.39***	–	–	–	–	–	–
May	0.0627	0.01	6.54***	–0.0354	0.00	–13.48***	–	–	–
June	–	–	–	–0.0528	0.00	–11.90***	–	–	–
July	0.0685	0.01	7.11***	–0.0319	0.01	–6.01***	–	–	–
August	0.0635	0.01	6.00***	–0.0573	0.01	–10.38***	–	–	–
September	–	–	–	–0.0287	0.00	–7.30***	–	–	–
October	–	–	–	–0.0280	0.00	–9.17***	–	–	–
November	–0.0406	0.01	–3.90***	–	–	–	–	–	–
December	–0.0749	0.01	–5.40***	0.0363	0.00	16.52***	–	–	–
Temperature	–	–	–	0.0044	0.00	8.98***	0.0025	0.00	5.62***
Rainfall	–0.0003	0.00	–7.86***	–	–	–	–	–	–
Sunshine	–0.0008	0.00	–5.09***	0.0001	0.00	3.00**	–0.0002	0.00	–3.03**
Trend	–0.0036	0.00	–6.43***	0.0009	0.00	2.74**	–0.0009	0.00	–5.26***
MAPE		6.9563			11.2856			8.3416	
MAE		0.0443			0.0155			0.0266	
R^2		0.754			0.761			0.564	

Note: AR=auto regression; SAR=seasonal auto regression; MAPE=mean absolute percentage error; MAE=mean absolute error; * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

October (late spring to mid fall, all $p < 0.001$) while the rates for December (early winter, $p < 0.001$) were higher. Again, as compared to other months, the admission rates for mixed/unspecified episodes were lower in February

(late winter, $p < 0.001$) and higher in March (early spring, $p < 0.001$). The R^2 within the ARIMA model was 0.761 for admissions for depressive episodes, and 0.564 for admissions for mixed/unspecified episodes.

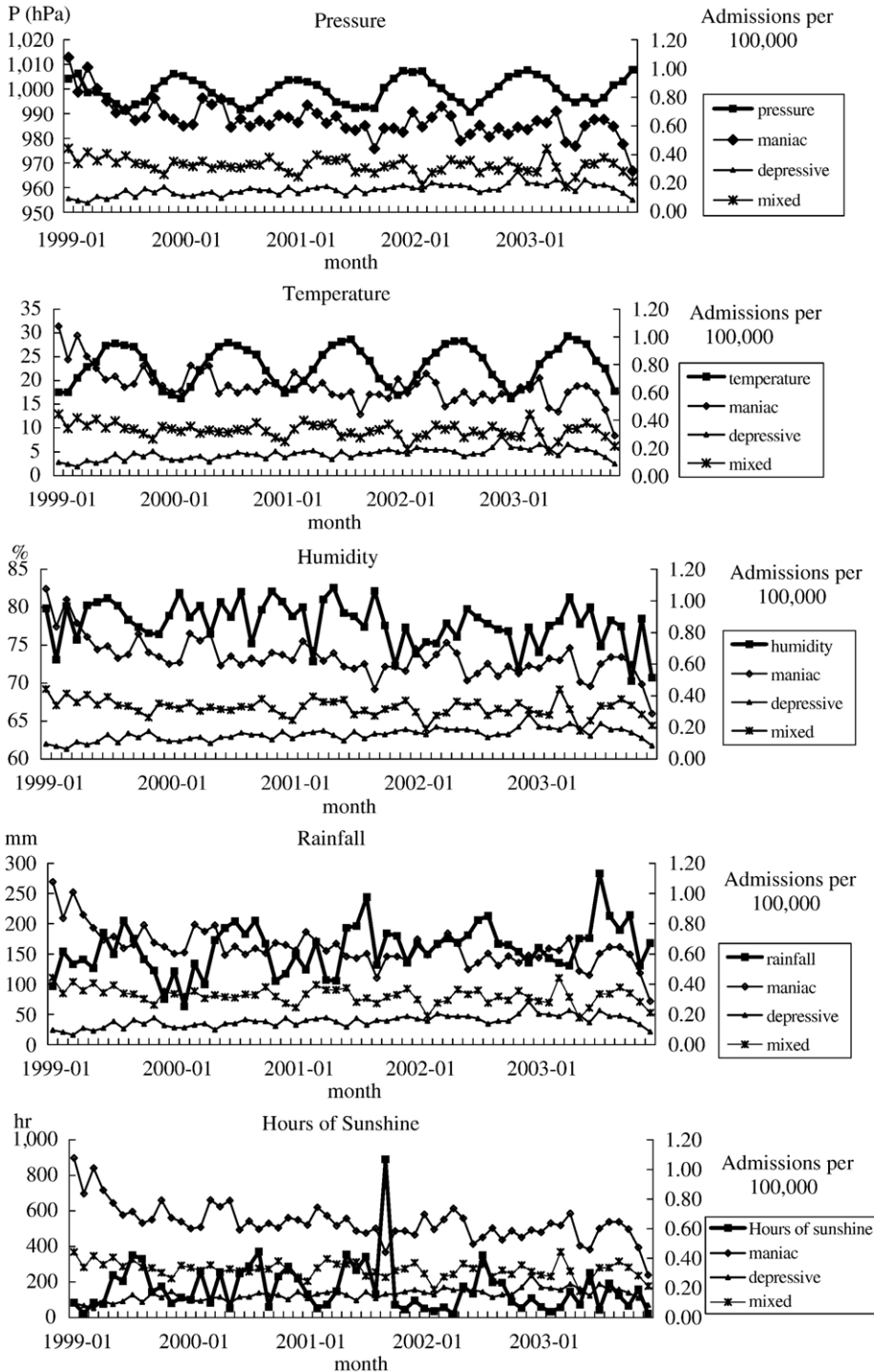


Fig. 2. Bipolar disorder admissions and climatic factors.

3.4. Climatic influence

Across the five-year study period, the mean monthly figures were ambient temperature of 23.1 °C, 77.9% relative humidity, atmospheric pressure of 999.48 hPa, 159.3 mm of rainfall, a maximum temperature of 26.8 °C, a minimum temperature of 20.4 °C, and monthly hours of sunshine of 161.0 (Table 1). The associations between the monthly admission rates for each subtype of bipolar disorder mood episodes and the monthly climate parameters are graphically illustrated in Fig. 2.

We can observe from the ARIMA regression models in Table 2 that the monthly admission rates for manic episodes have a negative association with both rainfall ($\beta = -0.0003$, $p < 0.001$) and hours of sunshine ($\beta = -0.0008$, $p < 0.001$), while the admission rates for depressive episodes have a positive association with temperature ($\beta = 0.0044$, $p < 0.001$) and hours of sunshine ($\beta = 0.0001$, $p < 0.01$), and those for mixed/unspecified episodes have a positive association with temperature ($\beta = 0.0025$, $p < 0.001$) and a negative association with hours of sunshine ($\beta = -0.0002$, $p < 0.01$).

4. Discussion

This study has used a five-year population-based dataset to examine seasonal variations in bipolar disorder admissions and to explore the association with climatic variations in Taiwan. The results indicate that significant seasonality is shown in all three subtypes of bipolar disorder mood episodes, although different seasonal patterns were observed in the admission rates. This is a finding which concurs with previous observations of seasonal variation in bipolar disorder admissions. A number of the prior studies have consistently reported variations in the incidence of bipolar disorder throughout the year in Europe, North America, New Zealand, Australia, India and Korea (Symonds and Williams, 1976; Frangos et al., 1980; Mulder et al., 1990; Barbini et al., 1995; D'Mello et al., 1995; Whitney et al., 1999; Avasthi et al., 2001; Lee et al., 2002).

To our knowledge, however, this is the first large-scale, population-based study so far conducted on the issue of seasonality in bipolar disorder among patients in a subtropical Asian climate. With its natural geographical boundary, surrounded as it is by sea, and its extremely low immigration rate, Taiwan provides us with a relatively fixed at-risk population for the entire period of this study. Furthermore, since 98% of the island's residents are of Han Chinese ethnicity, the composition of the population is generally quite

homogenous. These characteristics have therefore provided a much less biased background for us to test the hypotheses on the seasonality of bipolar disorder.

The results suggest a spring/summer peak in manic episodes, which finds general accord with a number of the prior studies conducted in Western countries (Symonds and Williams, 1976; Hare and Walter, 1978; Takei et al., 1992). However, based upon data from a teaching hospital in Bangalore, India (12° N), Jain et al. (1992) found no seasonal variation in admissions for mania, having assumed that seasonality may be masked in areas with a fairly constant climate. In contrast to that assumption, this study, along with the report by Kerr-Correa et al. (1998), provides confirmation of the existence of seasonality with regard to mania, even in subtropical areas, and also with variations in weather conditions of a much lower magnitude.

As compared to the seemingly robust finding across climatic zones of a spring/summer peak in manic episodes, if a peak does exist in admissions for depressive episodes, it has been discernible in the spring and fall seasons (Silverstone et al., 1995; Morken et al., 2002; Shapira et al., 2004). It seems that the seasonality of bipolar depression does vary between areas with different weather conditions. In terms of mixed/unspecified episodes, this study has found a seasonal pattern with an early spring peak, a finding which is at odds with the late summer peak found in the only other published research on mixed episodes, a study which was conducted in the US (Cassidy and Carroll, 2002).

This study has found that climatic variables such as rainfall, hours of sunshine and temperature have a significant association, in varying directions, with the admission rates for manic, depressive and mixed/unspecified episodes. In many of the prior studies, there has been a tendency to focus on an investigation into the relationship between monthly admission rates and the climatic parameters of the previous month (Mawson and Smith, 1981; Sayer et al., 1991; Salib and Sharp, 2002). Myers and Davies (1978), for example, assumed that climatic variables may act differently, with either prompt or delayed effects on the course of the mood episode. However, some of the more recent studies have shown that the climate of the current month is of greater relevance than that of the previous month (Lee et al., 2002; Shapira et al., 2004). Biomedical studies have also indicated that climate can have prompt effects on neurotransmitters connected with emotional regulation (D'Hondt et al., 1996; Lambert et al., 2002).

After controlling for trends and other seasonal factors in the ARIMA model, this study suggests a negative correlation between hours of sunshine and admission rates

for manic episodes, a finding which challenges the common notion that increasing amounts of sunlight can facilitate the incidence of manic episodes through the suppression of melatonin levels (Lewy et al., 1985; Nurnberger et al., 2000).

In line with the findings of Shapira et al. (2004), this study indicates a positive association between ambient temperature and the admission rates for depressive episodes. This relationship may not, however, exist in patients with unipolar depression. The relationship with climatic variables in mixed/unspecified episodes finds partial accord with that of manic episodes and similar partial accord with that of depressive episodes, which may reflect the mixed, yet distinct, properties of mixed or unspecified episodes.

The findings of this study need to be interpreted within the context of four limitations. First of all, admissions data should be used with caution, since the time lag between the onset of affective symptoms and admission to hospital could well be longer for both depressive and mixed episodes (Winokur, 1976). Furthermore, many bipolar patients with depressive or mixed episodes may not be admitted to hospitals, simply as a result of neglect, or because they may well lack the externalized disturbing behavior commonly seen among manic patients. These phenomena could confound the findings of this study.

Second, the psychiatric diagnoses, which rely on claims data reported by physicians or hospitals, may not cover co-morbid conditions and be less accurate than those made under a structured face-to-face interview schedule. Therefore, for mixed or unspecified episodes in particular, the diagnostic validity could compromise the findings.

Third, since those patients who were repeatedly hospitalized for mood episodes were more likely to receive psychotropic medication than those who were undergoing their first admission, the prophylactic effects of medication would alter the appearance of true seasonality (Clarke et al., 1999).

Finally, there may also exist some degree of ecological fallacy in the investigation of the relationship between aggregate data, such as climatic parameters and individual psychopathology (Sprinz, 2000). A very simple example of this is provided in the fact that some people prefer to stay indoors during the summer when it is hot and humid outdoors.

In conclusion, this study has clearly demonstrated seasonality among bipolar patients with different subtypes of mood episodes, even in a subtropical area with a fairly constant climate and with no obvious demarcation of the seasons. The seasonal variations in admission patterns, which

differ between manic, depressive and mixed/unspecified episodes, imply distinct scenarios in the onset of each subtype of mood episodes. The association between admission rates and certain climatic variables found in this study is informative and could pave the way for future studies aimed at exploring the influence of climate on the psychopathology of bipolar patients as well as the underlying mechanisms.

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