

## Correspondence

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### Research Letter

#### Changes in self-reported sleep duration predict mood changes in bipolar disorder

In a small pilot study of 59 patients with bipolar disorder, we found that a change in sleep duration (sleep plus bedrest) of  $>3$  h may signal that a large mood change is imminent, generally occurring on the next day (Bauer *et al.* 2006). Given the clinical importance of patient recognition of prodromal symptoms, we extended this analysis to a significantly larger sample.

Daily self-reported mood and sleep data were obtained from adult out-patients with a diagnosis of bipolar disorder by DSM-IV criteria, following the protocol for the pilot study (Bauer *et al.* 2006). At least 100 days of data with  $\leq 2$  sequential days of missing data was required for the analysis. All patients volunteered, provided informed written consent, and received treatment as usual throughout the study. Patients installed the previously validated Chrono-Record software in their native language on a home computer for data collection (Bauer *et al.* 2004). A 100-unit visual analogue scale was used to rate mood between the most extreme mania and depression the patient ever experienced. To record sleep, one of three icons was selected for each hour of the day: awake, asleep or bedrest, with awake as the default. Bedrest was defined as in bed but unable to sleep. From the self-reported data, a time series of daily mood and a time series of daily sleep duration data were created for each patient. The cross-correlation function (CCF) was used to analyse the relationship between these time series for each patient following the methodology described previously (Bauer *et al.* 2006). Each time series was filtered using an autoregressive integrated moving average model, ARIMA (0, 1, 1), to remove trends and establish stationarity before estimating the CCF from the residuals for time offsets of  $\pm 7$  days. An estimated CCF value greater than twice the standard error indicated the correlation was statistically significant from zero. Categorical demographic variables for patients with and without a significant CCF were compared using a  $\chi^2$  test. Continuous variables were compared using a univariate general linear model (GLM) with CCF significance and diagnosis included as fixed factors.

### Results

A total of 101 patients (67 female, mean age  $37.7 \pm 9.6$  years, 64 with bipolar I disorder and 37 with bipolar II disorder) completed the study, returning a mean of  $265 \pm 103$  days of data. The 101 patients included those in the pilot study, who provided additional data.

A significant negative cross-correlation was found between a change in sleep duration and a change in mood in 42 of the 101 patients (42%) for the day before or the day of the mood change, with 39% on the day before. With a negative cross-correlation, a decrease in sleep was followed by a shift in mood towards hypomania/mania and an increase in sleep was followed by a shift in mood towards depression. Considering all data from all patients, most changes in mood and sleep duration from one day to the next were small: 78.7% of all changes in sleep duration were  $\leq 2$  h in either direction, and 87.5% were  $\leq 3$  h. For changes in mood from one day to the next, 69.9% were  $\leq 5$  points in either direction, and 93.6% were  $\leq 20$  points. Patients with a significant cross-correlation between sleep duration and mood reported 65.6% of all sleep changes of  $>3$  h ( $\chi^2=118.2$ ,  $df=1$ ,  $p<0.001$ ), and 83.1% of all mood changes of  $>20$  points ( $\chi^2=488.5$ ,  $df=1$ ,  $p<0.001$ ). Patients with a significant cross-correlation between sleep duration and mood spent a smaller percent of days euthymic, and a larger percent of days depressed or manic (Table 1). While euthymic, mean sleep duration was not significantly different between those with and without a significant cross-correlation. However, while depressed, the mean daily increase in sleep duration for those with and without a significant cross-correlation was 1 h 18 min *versus* 6 min, respectively. While manic, the mean daily decrease in sleep duration was 1 h 12 min *versus* 18 min, respectively. Comparing demographic characteristics between patients with and without a significant cross-correlation, patients with a significant cross-correlation were more likely to be disabled (26.2% *versus* 10.2% respectively,  $\chi^2=4.499$ ,  $df=1$ ,  $p=0.034$ ), and to take benzodiazepines (63.6% *versus* 36.4% respectively,  $\chi^2=5.631$ ,  $df=1$ ,  $p=0.018$ ).

### Comment

These results confirm our prior pilot study findings of a significant, negative cross-correlation between a change in sleep duration and a change in mood with a 1 day latency in patients with bipolar disorder. These results also confirm that patients with a significant

**Table 1.** Mood and sleep duration for patients with and without significant negative cross-correlations

Mean percent of patient days	Cross-correlation						
	Not significant		Significant		Coefficient test <sup>a</sup>		
	%	<i>n</i>	%	<i>n</i>	<i>F</i>	df	<i>p</i>
Mania/hypomania	5.3	59	10.7	42	6.330	1, 98	0.013
Euthymic	81.4	59	63.8	42	13.877	1, 98	<0.001
Depression	13.3	59	25.4	42	9.719	1, 98	0.002
Severe mania	0.8	59	2.2	42	<sup>b</sup>		
Severe depression	3.0	59	8.7	42	8.136	1, 98	0.005
Sleep duration	Not significant		Significant		Coefficient test <sup>a</sup>		
	Hours	<i>n</i>	Hours	<i>n</i>	<i>F</i>	df	<i>p</i>
Mean while euthymic <sup>c</sup>	8.7	59	8.8	41	<sup>b</sup>		
Mean change from euthymic while depressed <sup>d</sup>	+0.1	38	+1.3	35	13.253	1, 70	0.001
Mean change from euthymic while manic <sup>d</sup>	-0.3	30	-1.2	26	7.490	1, 53	0.008

<sup>a</sup> Univariate GLM fixed factor.

<sup>b</sup> Estimated model not significant at the 0.05 level.

<sup>c</sup> One patient had no euthymic days.

<sup>d</sup> Not all patients had depressed or manic days.

cross-correlation experienced more symptoms, reporting two-thirds of all the sleep changes of >3 h, four-fifths of all large mood changes, and spending twice as much time both manic and depressed. No association was found between the mean sleep duration while euthymic and a significant cross-correlation. Similarly, in normal volunteers, vulnerability to neurocognitive impairment from sleep loss may have little relationship to an individual's basal sleep time (Van Dongen *et al.* 2004). Although sleep duration was indistinguishable while euthymic, patients with a significant cross-correlation had a large daily change from their mean euthymic sleep duration while depressed or manic, whereas those without a significant cross-correlation had little change in sleep duration while depressed or manic. Individual variability in sleep architecture may increase susceptibility to the impact of sleep changes on mood (Van Dongen *et al.* 2005), and represent a phenotype for bipolar disorder (Lenox *et al.* 2002).

A change in sleep duration of >3 h may signify an imminent mood change in patients with bipolar disorder. Although cross-correlation analysis can predict the order of sleep and mood changes, it cannot determine causality and many other factors including psychotropic medications may influence these events. Nevertheless, these results highlight the impact of a large sleep change on a vulnerable population, the

usefulness of sleep duration as a prodromal measure, and the importance of educating patients to closely monitor sleep patterns.

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## Letter to the Editor

### Why do psychotic patients take cannabis?

In spite of the strictures of Macleod (2007), previous research is generally in line with the report recently published by Degenhardt *et al.* (2007), which provides further evidence to challenge the hypothesis that psychotic patients take cannabis to ameliorate their symptoms. For example, in both the population-based study of Henquet *et al.* (2005) and in the large Dunedin birth cohort sample (Arseneault *et al.* 2002), psychotic symptoms failed to predict later cannabis use. Furthermore, the longitudinal cohort study from Christchurch, New Zealand specifically attempted to distinguish between the causal and self-medication hypotheses of cannabis use. The findings were that cannabis use increased risk of later psychosis, but the development of psychotic symptoms tended to decrease the subsequent consumption of cannabis (Fergusson *et al.* 2005).

However, in contrast with the above studies, Ferdinand *et al.* (2005) found that cannabis use predicted not only future psychotic symptoms in individuals who did not have such symptoms before they began using cannabis but also the reverse; the presence of psychotic symptoms in those who had never used cannabis predicted future cannabis use.

All the above studies have tried to disentangle self-medication, cannabis and psychosis, by applying sophisticated statistical techniques to longitudinal data. However, those studies did not directly ask psychotic patients or pre-psychotic patients why they smoked cannabis.

We know from the study of Arendt *et al.* (2007), in which cannabis-dependent subjects were actually asked why they used cannabis, that the most frequently reported reasons for using cannabis are relaxation, pleasure seeking and the experience of being 'high'. These reasons are similar to those given by cannabis users in the general population. Such effects may be particularly sought after in those with psychotic or quasi-psychotic symptoms. Kapur *et al.* (2005) asked a series of chronically treated psychotic patients how their antipsychotic medication affected their psychosis. Among the most common reported effects was that the medication 'helps me stop thinking' so that 'the symptoms do not bother me so much'. It is possible that from the patients' viewpoint cannabis use is beneficial in decreasing preoccupation with psychotic symptoms while not decreasing or even increasing them on objective measures.

Thus, the evidence of worsening of psychotic symptoms when using cannabis is not incompatible with the self-medication hypothesis, if what patients achieve when smoking cannabis is a detachment, as Kapur would call it, from their symptoms, even when they are rated as more severe on objective measures such as the BPRS.

### Declaration of Interest

None.

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