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Frontier of Psychiatry

Association Between Actigraphy Sleep Parameters and Subsequent Mood Episodes in Bipolar Disorder

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Abstract

Objective: Sleep disturbance is a core feature of bipolar disorder and also associated with mood symptoms. We investigated the association between actigraphy sleep parameters and mood episode relapses in patients with bipolar disorder.

Methods: A total of 193 outpatients with bipolar disorder who participated in the Association between the Pathology of Bipolar Disorder and Light Exposure in Daily Life (APPLE) cohort study were included in this prospective cohort study. The participants' sleep was objectively evaluated via actigraphy over 7 consecutive days for baseline assessment and then at the 2-year follow-up for mood episode relapses. Actigraphy sleep parameters were presented as the mean and variability (standard deviation) of each sleep parameter for 7 days.

Results: Compared with participants who did not have mood episodes during the follow-up, participants who had mood episodes showed significantly higher variability in total sleep time (median value: 66.0 vs. 49.0 min, respectively; $P< 0.001$), but there was no significant difference in the mean total sleep time (380 vs. 387 min, respectively). The

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Cox proportional hazards model adjusting for potential confounders showed that variability in total sleep time was significantly associated with an increase in mood episode relapses [per hour: HR, 1.407 (95%CI, 1.057-1.873)], mainly in depressive episodes [per hour: HR, 1.477 (95%CI, 1.088-2.006)].

Conclusion: Our findings suggest that consistency in sleep time might be helpful to prevent the relapse of mood episodes in bipolar disorder.

Keywords: bipolar disorder, sleep, variability, relapse, mood episode

Introduction

Bipolar disorder is a severe, recurrent mental disorder characterized by depressive episodes and manic or hypomanic episodes. Despite ongoing pharmacotherapy and psychotherapy, the relapse rate within two years exceeds 50%.[12] Therefore, it is important to identify factors associated with mood episodes in those with bipolar disorder.

Sleep disorders are frequently observed in patients with bipolar disorder, and are an important factor associated with mood episodes.[13] It has been reported that the need for sleep decreases during manic episodes, while insomnia or hypersomnia occurs during depressive episodes. Furthermore, sleep disorders have been reported to occur even in patients during periods of remission, who are not experiencing mood episodes.[10] Therefore, sleep disorders are recognized as a core feature of bipolar disorder.

However, there is debate regarding whether sleep disorders lead to the recurrence of mood episodes in patients with bipolar disorder. For example, multiple studies have reported that a decline in sleep quality, subjectively measured using sleep diaries or questionnaires, is significantly correlated with subsequent worsening of mood symptoms and an increase in the recurrence of mood episodes.[7][9][13] Conversely, recent studies reported no significant correlation between objective sleep parameters measured by actigraphy and the recurrence of mood episodes.[3][5] Therefore, further investigations using large sample sizes, long follow-up periods, and objective sleep parameters are necessary to clarify the relationship between sleep and the recurrence of mood episodes in bipolar disorder patients.

This study examined whether sleep, objectively measured using actigraphy, influences the recurrence of mood

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episodes in 193 patients with bipolar disorder.[4] We hypothesized that poor sleep quality, such as decreased mean sleep time and greater variability, would be associated with an increase in subsequent mood episodes.

I. Methods and Results

1. Methods

This study utilized data from the "Association between the Pathology of Bipolar Disorder and Light Exposure in Daily Life (APPLE) cohort study."[1] The inclusion criteria for participants were: aged 18–75 years, and diagnosed with bipolar I or II disorder according to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5). Night shift workers, those with a serious risk of suicide as judged by a clinician, and those with acute manic or depressive episodes were excluded. At the baseline, participants' demographic and clinical characteristics were assessed at the clinic, and then they were asked to perform the following actions at home for 7 consecutive days: (1) wear an actigraph (Actiwatch Spectrum Plus, Respironics, Pittsburgh, PA, USA) on the nondominant wrist throughout the day and night, except when bathing or performing aquatic activities, and (2) keep a sleep diary to record their bedtime and rising time each day. After the baseline assessment, we followed up on participants' mood episode relapses for 2 years. A total of 218 patients with bipolar disorder were enrolled in the APPLE cohort study. Among them, 18 participants with less than 3 days of sleep data were excluded, and 7 participants with a follow-up period of less than 6 months were also excluded. As a result, 193 participants were included in the final analysis. Written informed consent was obtained from all patients, and the study was approved by the Ethics Committee of Okehazama Hospital (H29-011).

Participants' sleep was assessed using an actigraph for 7 consecutive days, utilizing the following five sleep parameters: (i) sleep onset latency: the time between bedtime and sleep onset; (ii) wake after sleep onset: the time spent awake between sleep onset and sleep offset; (iii) total sleep time: the total time spent asleep between the start and end of sleep during the main sleep phase, excluding waking after sleep onset; (iv) sleep efficiency: the percentage of total sleep time between bedtime and rising time for the main sleep phase; (v) sleep midpoint: the mid-time between sleep onset and sleep offset. The mean and variability (standard deviation) were calculated for each sleep parameter.

Participants' mood episodes were assessed by their psychiatrists over a 2-year period following the baseline assessment. One and two years after the

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baseline evaluation, participants' psychiatrists were asked to diagnose the patients' mood episodes during the preceding year according to DSM-5 criteria. The time to relapse of a mood episode was calculated as the duration from the baseline assessment to onset of the first depressive episode, manic episode, or hypomanic episode.

All analyses were performed using SPSS version 25.0 for Windows (IBM Corp., Armonk, NY, USA). The time to mood episode relapse associated with sleep parameters was estimated using the Kaplan–Meier survival curve and Cox proportional hazards model. In the Cox proportional hazards model, we analyzed the sleep onset latency parameter using natural log-transformed continuous variables, given that it was not normally distributed. In the multivariable analysis, we calculated the hazard ratio by simultaneously adjusting the variables associated with mood episodes, including age, sex, residual mood symptoms, multiple mood episodes within the past year before the baseline assessment, bedtime, rising time, daytime physical activity, daytime illuminance, and night-time illuminance. A two-sided *p*-value of <0.05 was considered significant.

2. Results

Table 1 presents participants' baseline characteristics, including their demographic and clinical characteristics, and medication. The median age of the 193 participants was 44.0 (36.0–53.0) years, and 107 (55%) of them were female. Of the 193 participants, 176 (91%) completed the 2-year follow-up, and the median visit interval during the follow-up was 3.5 (2.2–4.3) weeks. During the 2-year follow-up period, 110 (57%) participants experienced mood episodes: 92 (47%) showed depressive episodes, and 49 (25%) experienced manic/hypomanic episodes. On considering mood episodes during the 2-year follow-up period, participants who had them were significantly younger than those who did not (42.5 vs. 47.0 years, respectively) and they had higher Montgomery–Åsberg Depression Rating Scale scores (10.0 vs. 5.0 points, respectively) and Young Mania Rating Scale scores (3.0 vs. 1.0 points, respectively), a higher rate of multiple mood episodes within the past year before baseline assessment (39 vs. 22%, respectively), later rising times (7:15 vs. 6:45, respectively), and lower daytime physical activity (154.6 vs. 182.5 counts/min, respectively).

Table 2 presents participants' actigraphy sleep parameters at the baseline. Participants who had mood episodes showed a significantly delayed mean midpoint of sleep (27:17 vs. 27:04,

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respectively) and greater variability in TST (66.0 vs. 49.0 min, respectively), SE (5.2 vs. 4.4%, respectively), SOL (15.0 vs. 10.9 min, respectively), and midpoint of sleep (40.2 vs. 31.9, respectively) than those who did not have them.

Figure 1 shows the total sleep time for each day in two representative patients who participated in this study. One patient experienced mood episode relapse during the follow-up period, whereas the other did not show such episodes. The two patients had almost the same intraindividual mean total sleep time across a week (360 vs. 370 min, respectively). However, the patient who showed relapsed mood episodes tended to exhibit marked fluctuations, with long sleep times on some nights and shorter ones on other nights. In contrast, the patient who did not experience mood episodes maintained a relatively constant sleep pattern from night to night.

Survival analyses using the Kaplan–Meier method indicated that the mean sleep onset latency and variability in total sleep time were significantly correlated with mood episode relapses. The mean estimated times to mood episode relapses were 12.5 and 16.8 months for higher and lower variability in total sleep time, respectively ($P < 0.001$).

The Cox proportional hazards models revealed that a higher mean sleep onset latency and midpoint of sleep and greater variability in total sleep time, sleep efficiency, and midpoint of sleep were significantly correlated with an increase in mood episode relapses (univariate model; Table 3). Variability in total sleep time remained significant in the model adjusted for age, sex, residual mood symptoms, multiple mood episodes within the past year before baseline assessment, bedtime, rising time, daytime physical activity, daytime illuminance, and night-time illuminance (per hour; hazard ratio [HR]: 1.407; 95% confidence interval (CI): 1.057–1.873; adjusted model; Table 3). Other parameters were not significant in the adjusted model (adjusted model; Table 3). Regarding the association between actigraph sleep parameters and subsequent depressive episodes, we found that a higher mean total sleep time, sleep onset latency, and midpoint of sleep and greater variability in total sleep time, SE, and midpoint of sleep were significantly correlated with an increase in depressive episode relapses (univariate model; Table 3). Although the mean midpoint of sleep and variability in total sleep time remained significant in the adjusted model, other parameters were not significant (adjusted model; Table 3). Significant correlations were found between the mean midpoint of sleep and variability in the total sleep time, sleep

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efficiency, and midpoint of sleep and manic/hypomanic episode relapses (univariate model; Table 3); however, they were not significant in the adjusted model.

II. Discussion

This study examined the association between actigraph sleep parameters and subsequent mood episodes in bipolar disorder patients. The results revealed that greater variability in total sleep time was significantly correlated with an increase in mood episode relapse, primarily depressive episodes. Additionally, a later midpoint of sleep was significantly correlated with depressive episodes.

These findings suggest potential adjunctive treatments for preventing the relapse or recurrence of mood episodes in those with bipolar disorder. Interpersonal and social rhythm therapy, which addresses interpersonal problems and disruptions in social rhythms, has been reported to be effective in preventing mood episodes in bipolar disorder patients.[6] Furthermore, a prospective cohort study of patients with bipolar disorder reported that the coexistence of circadian rhythm sleep-wake disorders, including irregular sleep-wake rhythm disorder, may be a significant predictor of mood episode relapse.[14] These previous studies and the present study suggest that maintaining consistent daily sleep-wake patterns may be useful as an adjunctive therapy for preventing the relapse and recurrence of mood episodes in patients with bipolar disorder. Furthermore, it has been reported that the degree of variability in sleep duration is associated with weight gain.[11] Since patients with bipolar disorder tend to be obese compared with the general population,[8] maintaining consistent daily sleep-wake patterns may be beneficial not only for mental health issues but also for physical health.

The most challenging aspect of this study was sample collection. As mentioned earlier, a total of 218 patients participated in this study, and more than 400 patients were actually recruited.[2] The first author handled almost all aspects of the study, including providing explanations, obtaining informed consent, and instructing patients on how to use the devices. It was particularly difficult for the author to personally visit patients' homes and workplaces to collect the research equipment (such as actigraphs). The actigraph measurement period was one week, and to ensure efficient device turnover, patients were asked to return the devices within two weeks. However, among patients whose condition was stable, many had appointments only once a month, and some were unable to

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return the devices to the hospital within two weeks. After careful consideration, I concluded that the author would personally collect the devices from patients who could not return them.

The most difficult part of collecting the devices was when I drove my personal car on the highway for an hour and a half one way to another prefecture to retrieve a device, only to be told by that patient that wearing the device was so uncomfortable they could barely keep it on. Looking back now, subsequently returning to the hospital, on the verge of tears, has actually become a fond memory.

One aspect I was particularly mindful of in this study was making sure to always express my gratitude to all the staff and patients involved. Conducting research while managing daily clinical duties results in an unbelievable workload. Consequently, during busy periods or when things did not go as planned, I would get frustrated and became prone to forgetting to thank the staff and patients who were cooperating with me.

However, the thing I was most conscious of when starting this study was to continue expressing my gratitude directly to them. The staff and patients who cooperated with me were doing so without compensation, and I believed that the study would not succeed unless I conveyed my gratitude to them. As a result, many people patiently cooperated with my research, and this study achieved a successful outcome.

Conclusion

This study revealed that the wide variability in total sleep time among patients with bipolar disorder is significantly and independently correlated with the relapse of mood episodes, particularly an increase in depressive episodes. As this was an observational study, further research involving randomized controlled trials is necessary.

Editor's Note: This paper is a Japanese adaptation of a recent research article[4] published in PCN, prepared at the request of the editorial committee and written by one of the authors, with additional commentary on its significance and future directions.

There are no conflicts of interest to disclose regarding this paper.

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表 1　193 名の参加者のベースライン特性

特徴	すべて（193 名）	フォローアップ中の気分エピソード		P 値
		あり（110 名）	なし（83 名）	
人口統計学的特徴				
年齢，年，中央値（四分位範囲）	44.0（36.0～53.0）	42.5（33.0～52.2）	47.0（39.0～57.0）	0.005
性別，女性，数	107（55.4%）	66（60.0%）	41（49.4%）	0.142
婚姻状況，数	101（52.3%）	52（47.3%）	49（59.0%）	0.105
教育歴（≥13 年），数	113（58.5%）	62（56.4%）	51（61.4%）	0.478
被雇用，数	79（40.9%）	39（35.5%）	40（48.2%）	0.083
臨床的特徴				
双極性障害のサブタイプ，Ⅰ型，数	69（35.8%）	39（35.5%）	30（36.1%）	0.921
双極性障害の発症年齢，年，中央値（四分位範囲）	31.0（22.2～39.7）	30.0（22.0～36.5）	33.0（24.0～42.0）	0.072
罹患期間，年，中央値（四分位範囲）	11.0（6.2～16.0）	10.0（6.5～6.0）	12.0（6.0～17.0）	0.335
MADRS スコア，ポイント，中央値（四分位範囲）	8.0（3.0～14.0）	10.0（5.0～15.0）	5.0（2.0～11.0）	<0.001
YMRS スコア，ポイント，中央値（四分位範囲）	2.0（0～5.0）	3.0（0～5.0）	1.0（0～3.0）	0.002
ベースライン評価前の前年の気分エピソード，数	61（31.6%）	43（39.1%）	18（21.7%）	0.010
就寝時刻，時刻，中央値（四分位範囲）	23:11（22:12～24:18）	23:15（22:15～24:35）	23:02（22:10～24:02）	0.127
起床時刻，時刻，中央値（四分位範囲）	7:00（6:13～7:48）	7:15（6:20～8:10）	6:45（6:02～7:33）	0.011
日中身体活動，回/分，中央値（四分位範囲）	168.6（131.1～222.4）	154.6（115.9～202.0）	182.5（145.8～235.3）	0.002
日中照度，ルクス，中央値（四分位範囲）	218.4（150.6～297.8）	207.1（141.0～286.1）	228.3（167.7～328.8）	0.112
夜間照度，ルクス，中央値（四分位範囲）	2.3（0.3～9.5）	2.6（0.4～9.4）	2.2（0.2～11.1）	0.740
フォローアップ完了，数	176（91.2%）	102（92.7%）	74（89.2%）	0.386
薬剤				
炭酸リチウム，数	78（40.4%）	46（41.8%）	32（38.6%）	0.647
抗てんかん薬，数	109（56.5%）	65（59.1%）	44（53.0%）	0.399
抗精神病薬，数	105（54.4%）	58（52.7%）	47（56.6%）	0.590
抗うつ薬，数	69（35.8%）	38（34.5%）	31（37.3%）	0.687
睡眠薬，数	122（63.2%）	71（64.5%）	51（61.4%）	0.658

データは中央値（四分位範囲）もしくは数（%）を表している．
MADRS：Montgomery-Åsberg Depression Rating Scale, YMRS：Young Mania Rating Scale.
（文献 4 を和訳して引用）

Table 1: Baseline characteristics of 193 participants

Characteristic

All (193)

Mood episodes during follow-up

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	Present (110)	Absent (83)	P-value
Demographic characteristics			
Age, years, median (interquartile range)			
Sex, female, number			
Marital status, number			
Years of education (≥13 years), number			
Employment status, number			
Clinical characteristics			
Bipolar disorder subtype, Type I, number			
Age at onset of bipolar disorder, years, median (interquartile range) Duration of illness, years, median (interquartile range)			
MADRS score, points, median (interquartile range)			
YMRS score, points, median (interquartile range)			
Mood episodes in the year prior to baseline assessment, number			
Bedtime, hours, median (interquartile range)			
Wake-up time, hours, median (interquartile range)			
Daytime physical activity, beats per minute, median (interquartile range)			
Daytime illuminance, lux, median (interquartile range)			
Night-time illuminance, lux, median (interquartile range)			
Follow-up completed, number			
Medications			
Lithium carbonate, number			
Antiepileptic drugs, number			
Antipsychotics, number			
Antidepressants, number			
Sleep medications, number			

Data are presented as median (interquartile range) or number (%).
MADRS: Montgomery–Åsberg Depression Rating Scale, YMRS: Young Mania Rating Scale.
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表 2　193 名のアクチグラフ睡眠パラメータ

特徴	すべて（193 名）	フォローアップ中の気分エピソード		*P* 値
		あり（110 名）	なし（83 名）	
平均，中央値（四分位範囲）				
総睡眠時間，分	385.1（334.6～433.3）	380.1（326.6～443.6）	387.0（350.3～431.1）	0.794
睡眠効率，%	83.6（77.6～87.6）	83.4（76.6～87.3）	84.1（79.3～88.6）	0.222
入眠潜時，分	16.0（9.2～26.0）	17.5（9.2～31.5）	13.5（9.0～20.4）	0.060
夜間中途覚醒，分	40.1（27.6～57.9）	40.5（25.4～60.8）	49.0（29.6～54.3）	0.956
睡眠中点，時刻	27:12（26:17～28:06）	27:17（26:30～28:17）	27:04（26:08～27:44）	0.035
ばらつき（標準偏差），中央値（四分位範囲）				
総睡眠時間，分	57.7（37.4～77.7）	66.0（45.0～92.8）	49.0（31.0～64.8）	<0.001
睡眠効率，%	4.8（3.3～7.8）	5.2（3.5～5.2）	4.4（2.9～6.8）	0.031
入眠潜時，分	13.6（7.7～21.4）	15.0（8.1～24.2）	10.9（6.9～17.2）	0.006
夜間中途覚醒，分	14.3（8.7～22.9）	14.0（10.7～21.9）	14.4（7.7～24.0）	0.671
睡眠中点，分	37.9（24.0～52.8）	40.2（24.6～58.8）	31.9（22.9～43.9）	0.009

データは中央値（四分位範囲）を表している．
（文献 4 を和訳して引用）

Table 2: Actigraph sleep parameters for 193 participants

Characteristics

All (193 participants)

Mood episodes during follow-up

Present (110 participants)

Absent (83 participants)

P-value

Mean, median (interquartile range)

Total sleep duration, min

Sleep efficiency, %

Sleep onset latency, min

Wake after sleep onset, min

Sleep midpoint, time

Variability (standard deviation), median (interquartile range)

Total sleep duration, min

Sleep efficiency, %

Sleep onset latency, min

Wake after sleep onset, min

Sleep midpoint, min

Data are presented as median (interquartile range).

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表 3　アクチグラフ睡眠パラメータと関連した気分エピソード再発のコックス比例ハザード分析

アクチグラフ睡眠パラメータ	気分エピソード				うつ病エピソード				躁/軽躁エピソード			
	単変量モデル		調整モデル		単変量モデル		調整モデル		単変量モデル		調整モデル	
	HR（95% CI）	*P* 値	HR（95% CI）	*P* 値	HR（95% CI）	*P* 値	HR（95% CI）	*P* 値	HR（95% CI）	*P* 値	HR（95% CI）	*P* 値
平均												
総睡眠時間，1 時間ごと	1.035 (0.911～1.176)	0.599	1.017 (0.886～1.195)	0.836	1.156 (1.009～1.324)	0.037	1.080 (0.910～1.282)	0.379	0.908 (0.748～1.102)	0.328	0.958 (0.749～1.226)	0.733
睡眠効率，1％ごと	0.984 (0.964～1.004)	0.111	0.984 (0.962～1.008)	0.187	0.984 (0.962～1.005)	0.140	0.985 (0.961～1.010)	0.231	0.985 (0.957～1.014)	0.295	0.992 (0.958～1.027)	0.664
入眠潜時，Log 分ごと	1.337 (1.030～1.737)	0.029	1.091 (0.829～1.437)	0.534	1.332 (1.010～1.755)	0.042	1.102 (0.827～1.468)	0.507	1.339 (0.965～2.029)	0.076	1.186 (0.789～1.783)	0.413
夜間中途覚醒，1 分ごと	1.004 (0.997～1.011)	0.280	1.007 (0.998～1.015)	0.118	1.006 (0.999～1.014)	0.086	1.009 (1.000～1.018)	0.057	0.998 (0.987～1.008)	0.637	0.999 (0.987～1.011)	0.903
睡眠中点，1 時間ごと	1.169 (1.051～1.300)	0.004	1.146 (0.989～1.328)	0.071	1.186 (1.059～1.330)	0.003	1.191 (1.023～1.387)	0.024	1.240 (1.086～1.416)	0.002	1.156 (0.947～1.411)	0.155
ばらつき												
総睡眠時間，1 時間ごと	1.733 (1.353～2.220)	<0.001	1.407 (1.057～1.873)	0.019	1.854 (1.420～2.421)	<0.001	1.477 (1.088～2.006)	0.013	1.729 (1.257～2.378)	0.001	1.369 (0.938～1.998)	0.104
睡眠効率，1％ごと	1.044 (1.004～1.085)	0.046	1.041 (0.995～1.089)	0.085	1.047 (1.003～1.093)	0.034	1.048 (0.997～1.101)	0.063	1.055 (1.006～1.107)	0.028	1.035 (0.975～1.099)	0.262
入眠潜時，Log 分ごと	1.588 (0.946～2.666)	0.080	1.378 (0.768～2.473)	0.768	1.618 (0.912～2.870)	0.100	1.405 (0.739～2.671)	0.299	1.354 (0.639～2.866)	0.429	1.180 (0.522～2.670)	0.691
夜間中途覚醒，1 分ごと	1.001 (0.987～1.014)	0.925	0.998 (0.983～1.014)	0.998	1.003 (0.989～1.017)	0.687	1.001 (0.984～1.017)	0.945	1.001 (0.981～1.021)	0.941	0.995 (0.972～1.019)	0.689
睡眠中点，1 時間ごと	1.266 (1.032～1.552)	0.023	1.112 (0.858～1.442)	0.422	1.325 (1.072～1.638)	0.009	1.192 (0.912～1.558)	0.199	1.397 (1.062～1.836)	0.017	1.144 (0.782～1.675)	0.488

ばらつきは 7 日間の睡眠パラメータの標準偏差を使用して計算された．睡眠潜時は自然対数変換後に解析された．調整モデルでは，年齢，性別，残遺気分症状，ベースライン前の前年中の気分エピソード，就寝時刻，起床時刻，日中身体活動，日中照度，夜間照度を含めて解析された．
（文献 4 を和訳して引用）

Table 3: Cox proportional hazards analysis of mood episode relapse associated with actigraph sleep parameters

Actigraph sleep parameters

Mood episode
  Univariate model
    HR (95% CI)
    P-value
  Adjusted model
    HR (95% CI)
    P-value

Depressive episode
  Univariate model
    HR (95% CI)
    P-value
  Adjusted model
    HR (95% CI)
    P-value

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Manic/hypomanic episode
  Univariate model
    HR (95% CI)
    P-value
Adjusted model
    HR (95% CI)
    P-value

Mean
 Total sleep duration, per hour
 Sleep efficiency, per 1%
 Sleep latency, per log minute
 Wake after sleep onset, per minute
 Sleep midpoint, per hour

Variability
 Total sleep duration, per hour
 Sleep efficiency, per 1%
 Sleep latency, per log minute
 Wake after sleep onset, per minute
 Sleep midpoint, per hour

Variability was calculated using the standard deviation of the 7-day sleep parameters. Sleep latency was analyzed after natural logarithmic transformation. The adjusted model included age, sex, residual mood symptoms, mood episodes in the year prior to baseline assessment, bedtime, wake-up time, daytime physical activity, daytime illuminance, and night-time illuminance.
(Translated and cited from Reference 4)

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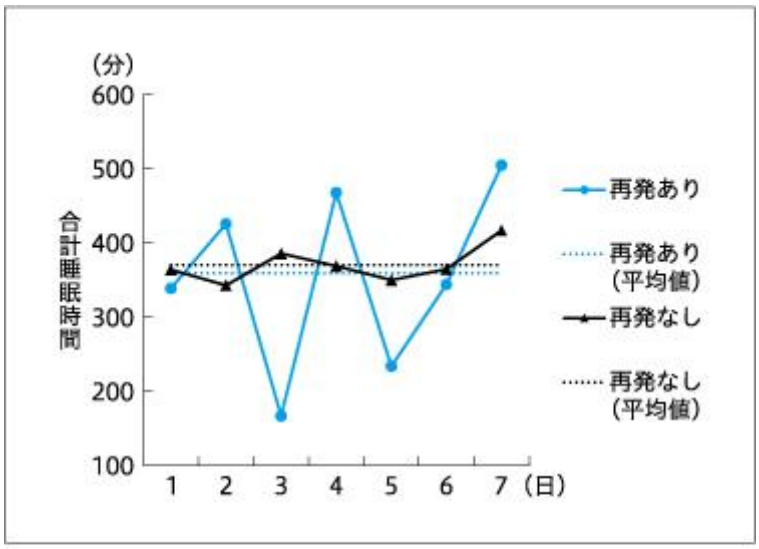

図 1　本研究に参加した代表的な 2 名の患者の 7 日間の総睡眠時間

青の実線は，追跡期間中に気分エピソードの再発を経験した患者の 7 日間の総睡眠時間を示し，青の点線は 7 日間の総睡眠時間の平均値を示す．黒い実線は，気分エピソードの再発を経験しなかった患者の 7 日間の総睡眠時間を示し，黒い点線は 7 日間の総睡眠時間の平均値を示す．
(文献 4 を和訳して引用)

Figure 1: Total sleep time for 7 days in two representative patients who participated in this study

The solid blue line indicates the total sleep time each day in the patient who experienced relapsed mood episodes during the follow-up period, whereas the dotted blue line indicates the mean total sleep time over 7 days. The solid black line indicates the total sleep time each day in the patient who did not experience mood episode relapse, whereas the dotted black line indicates the mean total sleep time for 7 days.

(Translated and cited from Reference 4)

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