久 留 米 大 学 文 学 部 紀 要
社会福祉学科編第10号・第11号合併号（2011）

Changes in rectal temperature rhythm on manic states of bipolar patients

Hiroo FUKUYAMA and Naohisa UCHIMURA

【Abstracts】 We investigated in the rectal temperature (RT) during a manic state measured in 6 patients with bipolar-1 was compared with that during remission measured in 4 of them. In addition, these values were compared with those in the normal controls. We measured the RT for 48-72 hours in their manic states. The acrophase in the RT rhythm during the manic state was advanced in 2 of 4 patients and delayed in 2, showing no consistant results. The average best fitted period was significantly shortened, and the amplitude of the RT was significantly increased during a manic state compared with the remission stage and the normal controls. And the average time of maximum temperature was significantly advanced during the manic state in the patients compared with the normal controls. The interval between the time of minimum temperature and the maximum temperature was shortened during the manic state compared with that in remission state. These results suggest that there are differences in the body temperature rhythm between manic and depressive states.

【Key words】 manic states, rectal temperature, rhythm disorder, body temperature rhythm

Introduction

Affevtive disorder patients commonly show biological rhythm-related symptoms, such as characteristic disturbances in the sleep-wake rhytms, diurnal mood changes, and a periodic pattern of symptom recurrence and remission. Since 1970s, many studies have suggested abnormalities in the biorhythm in affective disorders.[1–3] A substantial literature exists on this relationship in depressive disorders, and both insomnia and hypersomnia are diagnostic criteria for major depressive episode in DSM-IV-TR. Depressive patients commonly show biological rhythm-related symptoms, such as characteristic disturbances in the sleep-wake cycle, diurnal symptom changes, and a periodic pattern of symptom recurrence and remission Differences in sleep in bipolar and unipolar depression could conceivably be of use clinically, for example, in distinguishing between a unipolar and a bipolar depressive episode. Unfortunately, objective studies of sleep quality (using polysomnography, for example) in bipolar depression have generally found similar abnormalities in unipolar and bipolar depression, although limited data suggest that bipolar patients may have more early morning awakenings and greater total REM density than unipolar comparison subjects when matched for age, gender, and severity of symptoms.[3–25] Some clinicians believe that hypersomnia, rather than insomnia, is more indicative of bipolar than unipolar depression. However, a comparison of the hypersomnolence of bipolar depression with that of narcolepsy, using the Multiple Sleep Latency Test, an objective measure of excessive sleepiness, found no evidence of excessive daytime sleepiness in bipolar depression, which suggests that bipolar hypersomnolence is more reflective of anergia/fatigue than the true excessive leepiness seen in other primary sleep disorders. In particular, concerning depressive states of bipolar or monopolar affective disorders,

Table 1

	The least squares method				The observation method			
	The average best fitted period (hr.)	Mesor (℃)	Amplitude (℃)	Acrophase	Minimum temperature (℃)	The time of minimum temperature	Maximum temperature (℃)	The time of maximum temperature
Case1	22.4	37.18	0.435	12:02	36.6	2	37.7	12.5
Case2	21.8	36.75	0.438	15:34	35.8	3.5	37.4	13
Case3	22.2	37.04	0.458	12:27	36.3	2	37.7	12
Case4	24.1	37.05	0.581	17:21	36	2.5	38.2	18
Case5	24.1	37.7	0.455	13:26	35.7	3	37.9	13.5
Case6	22.1	37.18	0.66	15:06	36.8	3	38.3	12

Table 2

	The least squares method				The observation method			
	The least squares method (hr.)	Mesor (℃)	Amplitude (℃)	Acrophase	Minimum temperature (℃)	The time of minimum temperature	Maximum temperature (℃)	The time of maximum temperature
Case1	23.1	37.08	0.348	16:01	36.3	0.5	37.7	15
Case3	26.9	37.23	0.357	17:03	36.3	0	37.7	18
Case5	23.8	37.46	0.29	13:14	35.8	0.5	37.9	11.5
Case6	23.7	36.9	0.42	15:48	36.2	3	38.3	12

various biological hypotheses have been proposed such as the phase advancement hypothesis proposed, shortening of the REM latency, the phase instability hypothesis, or the beat hypothesis.[2,11,12,20] However, there have been only a few reports on manic states, which is a pathologic condition of similar affective disorders, in terms of the biorhythm.[15,18,19,24,26]

We evaluated the rectal temperature (RT) during a manic state in six patients with a bipolar affective disorder and also during remission in 4 of them.

Subjects and Methods

The subjects were 6 inpatients (4 males and 2 females) with a manic state (mean score on the Comprehensive Psychopathological Raring Scale for Mania; 45.2) of bipolar 1 type disorder (DSM-IV) and healthy adults volunteers (3 males and 3 females). The mean age was 54.7 years in the patient group and 53.3 years in the control group. After adequate explanation, informed consent was obtained from all subjects. The RT was measured continuosly for 48-72 hours after application of a rectal thermometer (Toyo Medical, Ltd.) that allows free movement in the psychiatric ward. In case 1, 3, 5, and 6, the RT was also measured during remission state in a similar manner. The controls performed daily activities as usual after application of a rectal thermometer. The RT rhythm was analyzed by the observation method and the least squares method. The average best fitted

Table 3

	The least squares method				The observation method			
	Minimum temperature (hr.)	Mesor (℃)	Amplitude (℃)	Acrophase	Minimum temperature (℃)	The time of minimum temperature	Maximum temperature (℃)	The time of maximum temperature
Manic state	22.70	37.28	0.502	13:45	36.35	2.5	37.90	12:30
Remission	24.33	37.17	0.354	15:02	36.40	1.0	37.85	14:08
	p<0.05		P<0.05					

period, amplitude, mesor, acrophase, the time of minimum and maximum temperature were evaluated.

Statiscal analysis was made between the manic state and the remission state and between the patients and control groups by Mann-Whitney's U test and paired t-test.

Results

1) The average best fitted period was significantly shortened, and the amplitude of the RT was significantly increased during a manic state compared with the remission state and the normal controls.

2) The mesor of the RT rhythm was higher during a manic state compred with the remission state and the normal controls.

3) The acrophase of the RT rhythm during the manic state was advanced in 2 of the 4 patients and delayed in 2, showing no consistent results.

4) The interval time of minimum temperature and the maximum temperature was shortened during the manic state.

Discussion

In this study, the RT during a manic state measured in 6 patients with manic-depressive illness was compared with that during remission measured in 4 of them. In addition, these value were compared with those in the normal controls.

There are many hypothesis on abnormalities of the rhythm in affective disorders such as the phase advancement hypothesis, and two-process model, but none of them has been established. Authers. reported changes in the biorhythm with the disordered acrophase in one case report with manic-depressive illness, i.e., delayed during depressive state and advancement during manic state. Some authers noted unstable acrophases of the biorhythm during manic states.[2,8,10,11,20,24]

In this study, the acrophase of the RT rhythm during a manic state was advanced in 2 patients but delayed in 2, and its direction could not be suggested. Therefore, further studies are necessary to determine whether the phase in the RT rhythm is unstable, or changes can not be clarified due to transverse

observation during a manic state.

The average best fitted period was significantly shortened during the manic state than during remission or in the normal controls. These findings were consistent with those during depressive states reported. Other stady about manic episode, the relationship between sleep and manic state involves the following aspects: 1)decreased need for sleep is a fundamental marker of the manic state; 2) sleep deprivation is one cause of mania and may in fact be a fundamental etiological agent in mania; 3) total sleep time is a predictor of future manic episodes; and 4) total sleep time may be a marker of response as well as a target of treatment in mania. It is possible that the average best fitted period is shortened in each phase of manic-depressive illness.

The amplitude of the RT was increased during the manic state compared with the remission state or the normal controls. And the mesor was higher during the manic state compared with the remission state or the normal controls. However, since activity is increased during manic state, the masking effects are also considered, and whether this finding reflects the internal clock mechanism cannot be determined. The observation method revealed shortening of the interval between the time of minimum temperature and the maximum temperature. This may be due to an acute increase in body temperature after rising in the morning. In general, duruing depressive state, the decrease in body temperature during night is slight, and therefore, a decrease in the amplitude of the RT and an increase in the mesor are observed. Such findings were not observed at least during manic states though depressive states were not evaluated in this study. This suggested there are differences in the body temperature rhythm between manic and depressive states.

Although sleep disturbance is a prominent feature of mania, its polysomnographic features have received little study. Further evaluation including that by polysomnography, genomic study is necessary in additional cases.[27–32)]

Our findings underline the importance of considering circadian system as a therapeutic target for the treatment of MD and developing specific therapeutic agents for unipolar and bipolar mood episodes.

References

1) Avery, D.H., et al., *Circadian temperature and cortisol rhythms during a constant routine are phase-delayed in hypersomnic winter depression*. Biol Psychiatry, 1997. 41(11): p. 1109-23.
2) Westrich, L. and J. Sprouse, *Circadian rhythm dysregulation in bipolar disorder*. Curr Opin Investig Drugs, 2010. 11(7): p. 779-87.
3) Taylor, M. A., *Circadian rhythms in manic-depressive psychosis*. Br J Psychiatry, 1970. 116(531): p. 239.
4) Sachar, E. J., *Twenty-four-hour cortisol secretory patterns in depressed and manic patients*. Prog Brain Res, 1975. 42: p. 81-91.
5) Kramer, B. A. and J. L. Katz, *Circadian temperature variation and depressive illness*. J Clin Psychiatry, 1978. 39(5): p. 439-44.
6) Kripke, D. F., et al., *Circadian rhythm disorders in manic-depressives*. Biol Psychiatry, 1978. 13(3): p. 335-51.
7) Halbreich, U., L. Grunhaus, and M. Ben-

David, *Twenty-four-hour rhythm of prolactin depressive patients*. Arch Gen Psychiatry, 1979. 36(11): p. 1183-6.

8) Wehr, T.A., et al., *Phase advance of the circadian sleep-wake cycle as an antidepressant*. Science, 1979. 206(4419): p. 710-3.

9) Pflug, B. and W. Martin, *[Analysis of circadian temperature rhythm in endogenous depressive illness (author's transl)]*. Arch Psychiatr Nervenkr, 1980. 229(2): p. 127-43.

10) Pflug, B., A. Johnsson, and A. T. Ekse, *Manic-depressive states and daily temperature. Some circadian studies*. Acta Psychiatr Scand, 1981. 63(3): p. 277-89.

11) Wehr, T. A., et al., *Circadian rhythm disturbances in manic-depressive illness*. Fed Proc, 1983. 42(11): p. 2809-14.

12) Wirz-Justice, A., *[Biologic rhythms and depression]*. Ther Umsch, 1983. 40(9): p. 763-8.

13) Wehr, T. A., et al., *Sleep and circadian rhythms in affective patients isolated from external time cues*. Psychiatry Res, 1985. 15(4): p. 327-39.

14) Avery, D.H., et al., *REM latency and core temperature relationships in primary depression*. Acta Psychiatr Scand, 1986. 74(3): p. 269-80.

15) Feldman-Naim, S., E.H. Turner, and E. Leibenluft, *Diurnal variation in the direction of mood switches in patients with rapid-cycling bipolar disorder*. J Clin Psychiatry, 1997. 58(2): p. 79-84.

16) Eiber, R. and M. Escande, *[Sleep electroencephalography in depression and mental disorders with depressive comorbidity]*. Encephale, 1999. 25(5): p. 381-90.

17) Boivin, D.B., *Influence of sleep-wake and circadian rhythm disturbances in psychiatric disorders*. J Psychiatry Neurosci, 2000. 25(5): p. 446-58.

18) Cervantes, P., et al., *Circadian secretion of cortisol in bipolar disorder*. J Psychiatry Neurosci, 2001. 26(5): p. 411-6.

19) Schreiner, R., et al., *Sleep and sleep-wake cycle in an 81-year-old patient with de novo ultra-rapid cycling bipolar disorder*. Eur Arch Psychiatry Clin Neurosci, 2001. 251(1): p. 29-31.

20) Wirz-Justice, A., *Biological rhythm disturbances in mood disorders*. Int Clin Psychopharmacol, 2006. 21 Suppl 1: p. S11-5.

21) Armitage, R., *Sleep and circadian rhythms in mood disorders*. Acta Psychiatr Scand Suppl, 2007(433): p. 104-15.

22) McClung, C.A., *Circadian genes, rhythms and the biology of mood disorders*. Pharmacol Ther, 2007. 114(2): p. 222-32.

23) Suzuki, K., et al., *Circadian variation of core body temperature in Parkinson disease patients with depression: a potential biological marker for depression in Parkinson disease*. Neuropsychobiology, 2007. 56(4): p. 172-9.

24) Salvatore, P., et al., *Circadian activity rhythm abnormalities in ill and recovered bipolar I disorder patients*. Bipolar Disord, 2008. 10(2): p. 256-65.

25) Salvadore, G., et al., *The neurobiology of the switch process in bipolar disorder: a review*. J Clin Psychiatry, 2010.

26) Fukuyama, H., et al., *A case of late onset rapid cycling affective disorder: changes in sleep pattern and rectal temperature in manic and depressive states*. Jpn J Psychiatry Neurol, 1993. 47(2): p. 452-4.

27) Benedetti, F., et al., *Actimetric evidence that CLOCK 3111 T/C SNP influences sleep and activity patterns in patients*

affected by bipolar depression. Am J Med Genet B Neuropsychiatr Genet, 2007. 144B(5): p. 631-5.

28）Soria, V., et al., *Differential association of circadian genes with mood disorders: CRY1 and NPAS2 are associated with unipolar major depression and CLOCK and VIP with bipolar disorder*. Neuropsychopharmacology, 2010. 35(6): p. 1279-89.

29）Sjoholm, L.K., et al., *CRY2 is associated with rapid cycling in bipolar disorder patients*. PLoS One, 2010. 5(9): p. e12632.

30）Lavebratt, C., et al., *CRY2 is associated with depression*. PLoS One, 2010. 5(2): p. e9407.

31）Lavebratt, C., et al., *PER2 variantion is associated with depression vulnerability*. Am J Med Genet B Neuropsychiatr Genet, 2010. 153B(2): p. 570-81.

32）Kripke, D. F., et al., *Genotyping sleep disorders patients*. Psychiatry Investig, 2010. 7(1): p. 36-42.