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Body Temperature and Mood Variations during Forced Desynchronization in Winter Depression: A Preliminary Report

Kathelijne M. Koorengevel, Domien G.M. Beersma, Marijke C.M. Gordijn, Johan A. den Boer, and Rutger H. van den Hoofdakker

Background: It has been suggested that certain abnormalities (e.g., in phase or amplitude) of the circadian pacemaker underlie seasonal affective disorder.

Methods: One male seasonal affective disorder patient (blind to the study design) participated in two 120-hour forced desynchrony experiments and was subjected to six 20-hour days, once during a depressive episode and once after recovery. Core body temperature was continuously measured. During wakefulness, the Adjective Mood Scale was completed at 2-hour intervals.

Results: Sleep–wake as well as pacemaker-related variations of mood were found, both when the subject was depressed and when he was euthymic. Compared with recovery, during the depressive episode the circadian temperature minimum and the circadian mood variation showed phase delays of approximately 1 and 2 hours, respectively.

Conclusions: The data of this first seasonal affective disorder patient, participating in forced desynchrony experiments, may indicate a phase delay of the circadian pacemaker during a seasonal affective disorder episode. Biol Psychiatry 2000;47:355–358 © 2000 Society of Biological Psychiatry

Key Words: Seasonal affective disorder, mood, circadian rhythms, phase shift, forced desynchronization, light therapy

Introduction

The circadian pacemaker, or biological clock, is localized in the suprachiasmatic nucleus of the brain and is known to regulate seasonal changes in a variety of animal behaviors (e.g., reproduction and hibernation). It serves as an internal timing mechanism with a period of approximately 24 hours. The environmental light–dark cycle is the most important cue for synchronization of the circadian system to the habitual 24-hour sleep–wake cycle. Therefore, the seasonal manifestation of depressive symptoms and the efficacy of light therapy might suggest involvement of the human circadian pacemaker in seasonal affective disorder (SAD). Core body temperature exhibits a pronounced 24-hour variation and is often the object of study in human circadian rhythm research; however, the effects of daily activities on core body temperature mask its overt circadian rhythm. There are two ways to measure the characteristics of the circadian pacemaker, by either experimentally controlling or mathematically correcting for masking effects on core body temperature. First, under the controlled conditions of wakefulness with the subject in supine posture, low light intensity, and isocaloric snacks of the constant routine protocol, circadian amplitude and phase can be accurately determined. Such studies have shown that the dim-light melatonin onset and certain characteristics of the circadian temperature rhythm were phase delayed in female SAD patients compared with those in controls (Dahl et al 1993; Wirz-Justice et al 1995). A disadvantage of constant routine protocols is that subjects are deprived of sleep as they have to stay awake for more than 24 hours. As in nonseasonal major depressive disorder, in SAD this deprivation may lead to changes in mood (Graw et al 1998), which in turn can have an influence on overt rhythms. Therefore, the second method of forced desynchronization could be more appropriate. When subjects are forced to be awake and sleep on an artificial day length (e.g., 20 or 28 hours), outside the range of entrainment of the human circadian system, the circadian pacemaker characteristics can be separated from those dependent on sleep or time awake, without sleep deprivation interfering. Healthy subjects subjected to a forced desynchrony protocol show a complex and nonadditive influence of circadian phase and duration of prior wakefulness on subjective mood (Boivin et al 1997). We thus subjected one male SAD

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patient to a forced desynchrony protocol to study the pacemaker characteristics and the circadian and sleep-wake-dependent variations of mood, during a depressive episode and after good response to light treatment in the winter of 1997–1998. To the best of our knowledge, this is the first application of this technique to depression.

Methods and Materials

The subject, who met the DSM-IV criteria for recurrent major depression with seasonal pattern (American Psychiatric Association 1994) and the Rosenthal criteria for SAD (Rosenthal et al 1984), was a 54-year-old male outpatient, known to respond favorably to light treatment. He was in good physical health, did not use any medication at least 1 month before the experiments (especially no psychotropic medication in the previous 6 months) and smoked approximately 15 cigarettes a day. The subject gave written informed consent to the protocol, approved by the Medical Ethics Committee of the Academic Hospital Groningen.

During the winter season, the Beck Depression Inventory (BDI) (Beck et al 1961) and the Structured Interview Guide for the Hamilton Rating Scale of Depression (HAM-D), Seasonal Affective Disorder self-rating version (SIGH-SAD-SR; Williams et al 1992) consisting of the 21-item HAM-D and an additional eight-item atypical symptom scale (ATYP) were completed weekly. A BDI score of $\geq 16$ was required for inviting the patient to participate during the depressive episode. A BDI score of $< 6$ was required for participation following response to light treatment. After 4 baseline days at home, in which sleep was scheduled between midnight and 8:00 AM (verified by wrist actometry), the patient entered a temporal isolation unit in which no information on the time of day was available. Following one habitation night in this temporal isolation unit, he was subjected to a 120-hour forced desynchrony protocol (six 20-hour “days”; see Hiddinga et al 1997). The subject, blind to clock time and the timing of the sleep–wake schedule, lived under an artificial 20-hour light–dark schedule consisting of 13.5 hours of wakefulness in dim light ($< 10$ lux) and 6.5 hours of darkness, during which he had to be in bed. Core body temperature data were stored at 1-min intervals. Every 2 hours the Adjective Mood Scale (AMS; Von Zerssen 1986)—ranging from 0, not depressed, to 56, severely depressed—was completed to monitor mood. The circadian variation of mood was computed by calculating the mean score of all AMS questionnaires completed at specific real clock times. To adjust the computed circadian mood variation for the sleep–wake-related variation of mood, the mean sleep–wake-dependent variation at specific times of the subjective day was subtracted from the raw AMS scores first. In a similar way, the sleep–wake-related variation of mood was obtained by calculating the mean scores of AMS ratings obtained per specific time of the subjective day. In turn, before computing the sleep–wake-related variation of mood and SDs, the mean circadian variation at specific real clock times was subtracted from the raw AMS data to adjust for the circadian-related mood variation. During the 4 baseline days and in temporal isolation, a subjective sleep quality questionnaire, with scores ranging from 0 (high quality) to 14 (low quality) was completed after each period of sleep (Mulder-Hajonides van der Meulen et al 1980).

Results

The first experiment was conducted in November 1997. At baseline, the subject’s BDI score was 15; after the experiment the score was 18 (SIGH-SAD-SR 24 and 32; HAM-D 17 and 22, ATYP 7 and 10). The BDI score was 7 (SIGH-SAD-SR 11; HAM-D 8, ATYP 3) 7 days after finishing subsequent light treatment (5 consecutive days of 30-min 10,000-lux light in the morning). The second experiment was conducted in January 1998, when the BDI score was 5. After the experiment, it was 3 (SIGH-SAD-SR 9 and 18; HAM-D 5 and 11, ATYP 4 and 7). Until the end of winter, the BDI score remained 5 or less (SIGH-SAD-SR $\leq 10$). The temperature data were analyzed by an iterative method (Hiddinga et al 1997). It showed an endogenous circadian rhythm period ($\tau$) of 23 hours 38 min during the depressive episode and one of 24 hours 4 min after recovery. The circadian temperature minimum, defined as the mid-point between the upward and downward crossings through the average value of the temperature curve smoothed by spline approximation, was reached at 5:13 AM and 4:16 AM on the first day of the forced desynchrony protocol, respectively. The absolute AMS scores
The circadian variation of mood (mean and SD) is double plotted (Figure 1). In both experiments, the $\tau$ values (as determined from body temperature data) were close to 24 hours. Over the entire protocol, the difference with a 24-hour period did not accumulate to more than 2 hours, which is the interval between successive mood ratings. A linear regression analysis, using a 24-hour sine function, was thus applied to the circadian variation of mood observed in both conditions. This analysis revealed a significant circadian variation, both in the depressed state ($\tau = 24.445, p = .014$) and in the remitted state ($\tau = 24.394, p = .037$). Both curves reveal peaks in depression scores in the early morning hours. Cross-correlation suggests that the circadian variation of mood during depression is phase delayed by approximately 2 hours as compared with recovery. Figure 2 presents the sleep–wake-related variation of subjective mood as a function of time since awakening (mean and SD). In both conditions, a steady deterioration of mood is apparent, without indications of a phase difference. The sleep quality score (mean $\pm$ SD) was 6 $\pm$ 2 at times of the depressive episode and 2 $\pm$ 2 in the remitted state, with ranges of 4–8 and 0–5, respectively. In temporal isolation, the sleep quality score (mean $\pm$ SD) was 6 $\pm$ 5 (range 1–13) in the depressed and 6 $\pm$ 4 (range 2–13) in the remitted state.

**Discussion**

Before and after the forced desynchrony experiments, the BDI scores did not reveal systematic trends in depressed mood in both conditions. The observed changes in SIGH-SAD-SR scores during the experiment are primarily a consequence of an accompanied increased appetite and a low sleep quality.

The $\tau$ values obtained from the two experiments with this SAD patient lie within the range of $\tau$ values found in healthy subjects (Hiddinga et al 1997). Czeisler et al (1999) recently reported $\tau$ values of 24.18 $\pm$ 0.04 hours in both young and older subjects participating in a forced desynchrony study. A comparison with Hiddinga et al (1997) and Czeisler et al (1999) reveals that the difference in $\tau$ values found in the depressed and remitted state is likely due to the less accurate 120-hour forced desynchrony protocol and probably not so much to intra- or interindividual differences. As a consequence, a larger group of subjects is required to demonstrate systematic differences between SAD patients and healthy controls.

We observed circadian and sleep–wake-related variations of mood. The magnitudes of the variations are similar for the two conditions. The demonstrated nadir of circadian mood modulation in the early morning hours and the deterioration of mood during cumulative wakefulness are consistent with observations in healthy subjects (Boivin et al 1997). Compared with recovery, there is support for the existence of a phase delay of the circadian temperature minimum and of subjective mood during the depressive episode. The subject received 1 week of light treatment after participation in the first experiment. The second experiment was conducted 6 weeks after finishing the treatment week. Thus, the results cannot be considered as a masking effect of light per se; however, in temporal isolation, subjective sleep quality showed a wide variation in both experiments. This may have influenced the computed periods of the pacemaker, the observed phase of the circadian temperature minimum, and the sleep–wake- as well as the pacemaker-related mood variation. More data are presently being collected to clarify whether the manifestation of SAD and the efficacy of its treatment are associated with phase shifts of the circadian pacemaker.

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**References**


**Figure 2.** Double plot of the sleep–wake-related variation of subjective mood (mean Adjective Mood Scale [AMS] score and SD), monitored every 2 hours during 13.5 hours of wakefulness of the 20-hour subjective day, in one male seasonal affective disorder patient, subjected to two 120-hour forced desynchrony experiments, once during a depressive episode (black circles) and once 6 weeks after recovery upon 1 week of light therapy (open squares).