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Mood regulation in seasonal affective disorder patients and healthy controls studied in forced desynchrony

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Abstract

In healthy subjects, both the duration of wakefulness and the circadian pacemaker have been demonstrated to be involved in the regulation of mood. Some features of affective disorders suggest that these two factors also play a role in the dysregulation of mood. In particular, disturbances of the circadian pacemaker have been proposed to be a pathogenetic factor in Seasonal Affective Disorder, winter type (SAD). This report presents a test of this proposition. To this end seven SAD patients and matched controls were subjected to a 120-h forced desynchrony protocol, in which they were exposed to six 20-h days. This protocol enables us to discriminate the extent to which the course of mood is determined by the imposed 20-h sleep–wake cycle from the influence of the circadian pacemaker on that course. Patients participated during a depressive episode, after recovery upon light therapy and in summer. Controls were studied in winter and in summer. Between SAD patients and controls no significant differences were observed in the period length nor in the timing of the endogenous circadian temperature minimum. In both groups, sleep–wake cycle- and pacemaker-related components were observed in the variations of mood, which were not significantly different between conditions.

Keywords: Circadian pacemaker; Sleep–wake cycle; Melatonin; Core body temperature; Depressive mood

1. Introduction

In major depression, a diurnal variation of mood and a temporary alleviation of symptoms by the deprivation of sleep have often been observed. These clinical features gave rise to several hypotheses relating to the involvement of processes controlled by the circadian pacemaker, the sleep–wake cycle, or an interaction between these processes in the dysregulation of mood (reviewed in, for example, Van den Hoofdakker, 1994; Wirz-Justice, 1995; Buysse et al., 1999; Boivin, 2000). In the present experiment the regulation of mood in seasonal affective disorder, winter type (SAD) is explored, specifically the contributions of the

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circadian pacemaker and the sleep–wake cycle to this regulation.

The strongest evidence for the involvement of the duration of prior wakefulness in the regulation of mood has been found in sleep deprivation experiments. In depressed patients, sleep deprivation often results in a pronounced improvement while recovery sleep is frequently followed by relapse (Wirz-Justice and Van den Hoofdakker, 1999). In contrast, healthy subjects experience a deterioration of mood when they are deprived of sleep (Gerner et al., 1979; Brendel et al., 1990). Thus, the regulation of mood is affected by manipulation of the sleep–wake cycle in both depressed patients and controls.

Hypotheses about the involvement of abnormal functioning of circadian processes in depression have especially gained interest with respect to SAD. As in non-seasonal depression, in SAD both diurnal variation (Graw et al., 1991; Krauss et al., 1992) and a sleep deprivation-induced improvement of mood (Graw et al., 1998) have been observed. The annual recurrence of depressive symptoms in autumn and/or winter (Rosenthal et al., 1984) and the efficacy of bright light therapy (Terman et al., 1989) provide additional support for the involvement of the circadian pacemaker in this disorder. The pros and cons concerning proposed circadian explanations of the pathogenesis of depressive disorders including SAD are described more extensively by Boivin (2000).

The human circadian pacemaker, localized in the suprachiasmatic nuclei of the brain, generates endogenous physiological and psychological rhythms with a near 24-h period (Campbell et al., 1993; Czeisler et al., 1999). The daily exposure to light synchronizes these endogenous circadian rhythms with the exogenous 24-h light–dark cycle (Boivin et al., 1996; Jewett et al., 1997). Thus, the pacemaker enables adequate adaptation to the alternation of light and darkness caused by the earth's rotation and is involved in the regulation of seasonal changes in behavior. It has been postulated that a phase delay of the circadian pacemaker relative to the timing of the sleep–wake cycle underlies the pathogenesis of SAD (Lewy et al., 1987) and that an advance phase shift is required for improvement (Lewy et al., 1998; Terman et al., 2001). According to this phase-shift hypothesis, light therapy applied in the morning is effective because of its phase-advancing properties. Alternatively, the amplitude hypothesis (Czeisler et al., 1987) postulates that SAD patients might show a diminished circadian amplitude and that the amplitude-enhancing effect of light applied in daytime accounts for the efficacy of light therapy in SAD.

Overt circadian rhythms always represent a mixture of circadian pacemaker and sleep–wake-related processes. Constant routine and forced desynchrony protocols have been designed to reveal unmasked circadian rhythms. In the constant routine (CR) protocol, participants are subjected to a regime of more than 24 h of wakefulness in dim light. Subjects stay in a semi-recumbent position. Hourly iso-caloric snacks provide a constant energy supply (Mills et al., 1978; Czeisler et al., 1985). Physiological circadian rhythms measured under these constant conditions are considered to reflect unmasked circadian pacemaker activity. In a forced desynchrony (FD) protocol, subjects are living on a schedule of artificial 'days' that are either shorter or longer than 24 h, i.e. 20 or 28 h (Kleitman and Kleitman, 1953; Czeisler et al., 1986). In the present study artificial days lasted 20 h: 13.5 h of wakefulness in dim light (<10 lux) and 6.5 h of darkness in which subjects could sleep. In dim light, the circadian pacemaker is not able to adapt to this unusual schedule of wakefulness and sleep and starts to oscillate according to its endogenous period (Klerman et al., 1996), which is close to 24 h (Campbell et al., 1993; Czeisler et al., 1999). As a result of the desynchronization between the sleep–wake cycle and the circadian pacemaker, the scheduled activities occur at all endogenous circadian phase positions. The contributions of the sleep–wake cycle and the pacemaker to the circadian variation of a variable can be disentangled by a mathematical method (Dijk et al., 1992; Hiddinga et al., 1997).

So far, two CR studies have been performed in female SAD patients and matched controls. In both studies, certain characteristics of the circadian rhythm in body temperature (Dahl et al., 1993; Wirz-Justice et al., 1995), melatonin (Dahl et al., 1993) and cortisol (Avery et al., 1997) were shown