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Bright White Light Does Not Improve Narcoleptic Symptoms

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Summary. Bright white light (500 lx) for 4 h/day was applied to seven narcoleptic patients (age 47–65 years, mean 55 years). The effects of the light on the disturbed sleep-wake cycle in narcoleptics were investigated by the measurement of the following parameters: (1) excessive daytime sleepiness and sustained attention (multiple sleep latency test); (2) rest-activity cycles; (3) self-ratings (mood, anxiety, tiredness); (4) urinary cycles of 6-OH melatonin sulphate and cortisol; (5) sleep EEG. Treatment with bright light showed neither objective nor subjective changes in the clinical symptoms of narcolepsy. While similar "dosage" light applications can phase shift human circadian rhythms and improve depression and hypersomnia in winter depression, it is not an appropriate treatment for narcolepsy.

Key words: Narcolepsy – Bright white light – Circadian rhythms

Introduction

Are circadian rhythms involved in the pathophysiology of narcolepsy? [14, 19, 20] There is a high correlation between the first manifestation of the illness and a socially induced shift in the usual sleep-wake rhythm [17, 18, 21]. Sleep onset REM episodes characteristic of narcolepsy are often found when the sleep-wake cycle is delayed, as under conditions of temporal isolation [29] or westward transmedian flight. Melatonin, the neurohormone of the pineal gland, is an excellent phase marker for the circadian pacemaker in the suprachiasmatic nucleus [15]. Abnormal melatonin rhythms in narcoleptics have been found in one study [2], but not replicated [3]. However, the function of the suprachiasmatic nucleus and a number of rhythms driven by it are not modified in the canine model of narcolepsy [24].

Sleep regulation has been modelled by the interaction of a sleep-wake independent circadian pacemaker (process "C") with a sleep-wake dependent process "S" [4]. Bright light can shift the circadian pacemaker independent of the sleep-wake cycle [8, 13, 16]. Thus bright light is a tool both for theoretical investigation and for therapeutic intervention in sleep disturbances related to disorders of circadian rhythms (e.g. shift work, jet lag [7, 9, 10, 16]. It has been successfully used to treat seasonal affective disorder, a periodically recurring winter depression characterised by excessive fatigue and hypersomnia [16, 23, 25, 27, 28]. Since light therapy reduces the excessive sleep need in seasonal affective disorder patients, we initiated a trial in narcoleptic patients. Not only could bright light to be a potential therapy, but the experiment would clarify whether a circadian disturbance was of aetiological significance in narcolepsy.

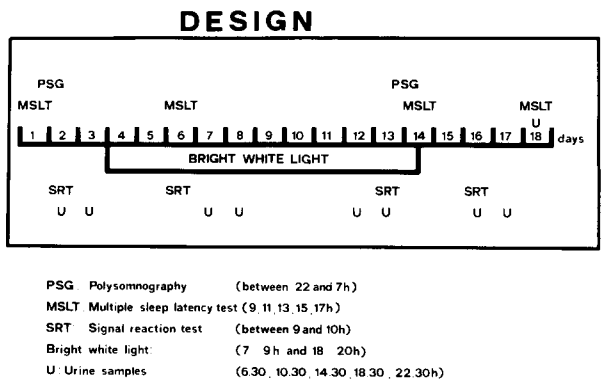

Fig. 1. Study design

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Patients and Methods

Seven patients (6 men, 1 woman, aged 47–65 years), with narcolepsy established by the criteria of Honda [12] (presence of cataplexy, sleep attacks and sleep onset REM periods), participated in the study, which was carried out in November-December 1986. Stimulants were stopped 21 days beforehand (1 patient continued with propranolol); three additionally ceased taking tricyclics. The experimental protocol is summarised in Fig. 1. After 3 days baseline, bright white light (5000 lx twice a day, 7–9 a.m. and 6–8 p.m.) was administered for 10 days, followed by a 4-day period without bright white light. Polysomnography was carried out at baseline and at the end of the light treatment, and visually analysed by conventional criteria [22]; qualitative estimation of diurnal vigilance was done by means of the standardised multiple sleep latency test (MSLT) and a psychophysiological optical vigilance test (signal reaction test). Behavioural rest-activity cycles were recorded

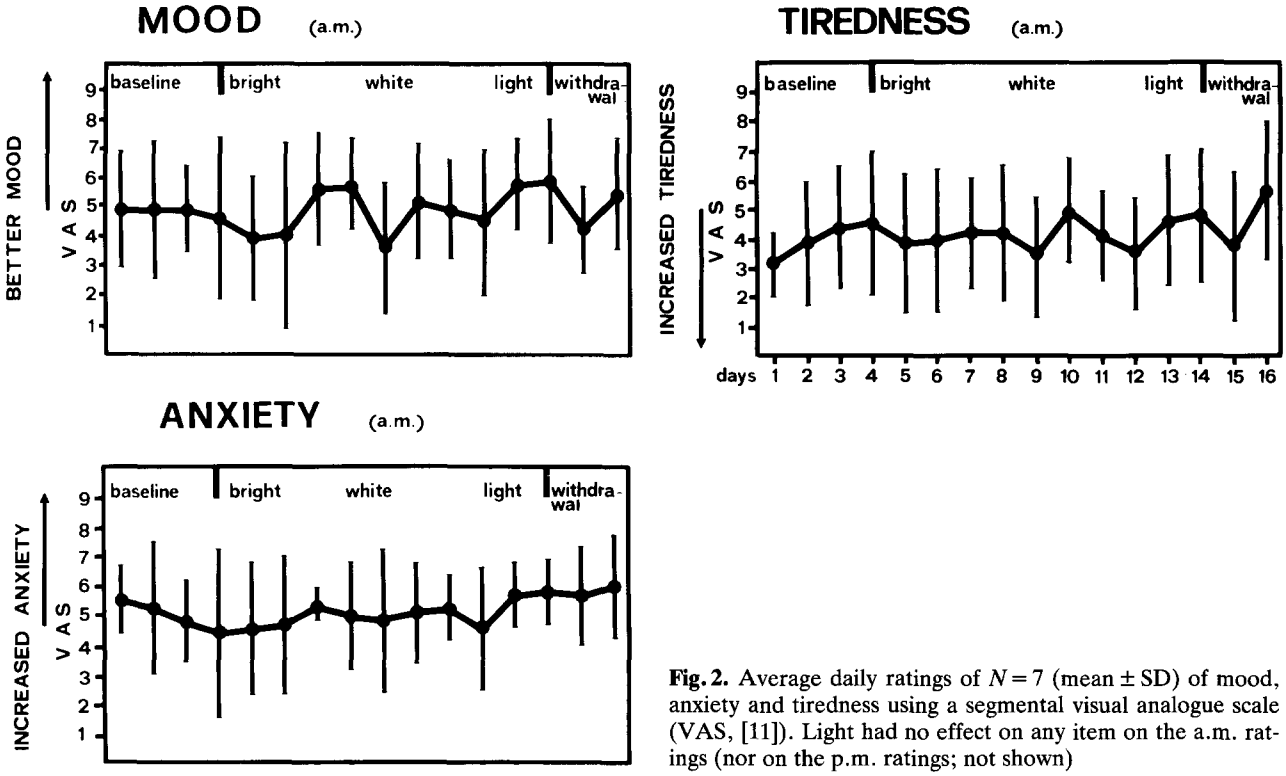

Fig. 2. Average daily ratings of $N = 7$ (mean ± SD) of mood, anxiety and tiredness using a segmental visual analogue scale (VAS, [11]). Light had no effect on any item on the a.m. ratings (nor on the p.m. ratings; not shown)

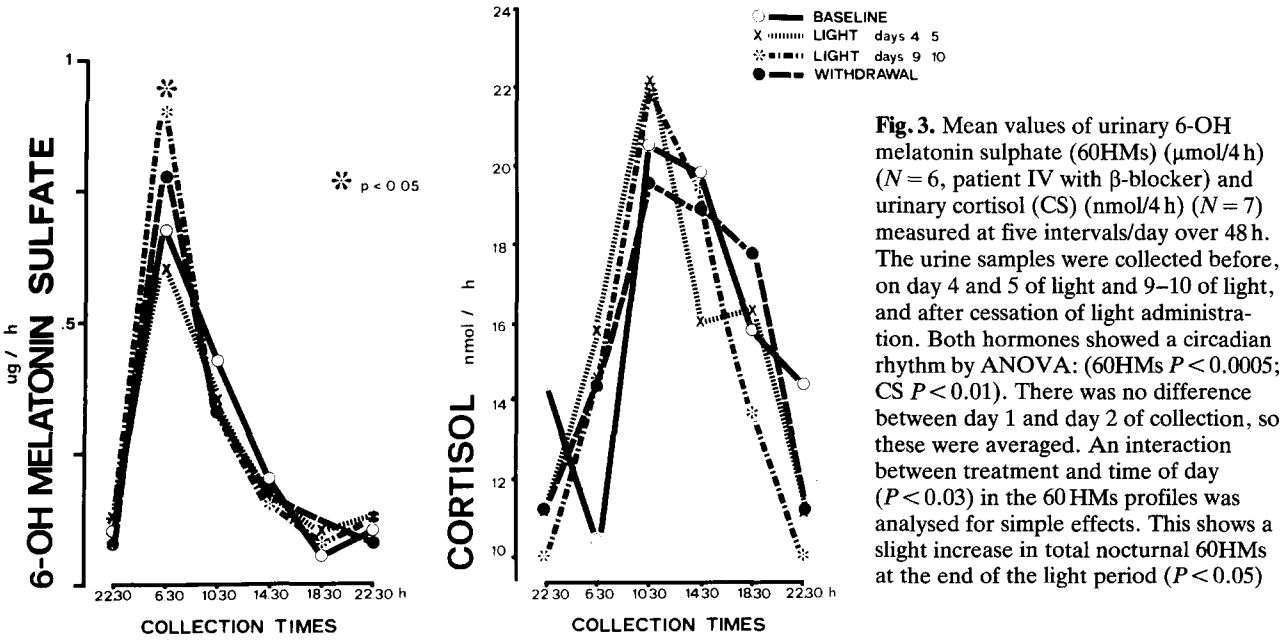

Fig. 3. Mean values of urinary 6-OH melatonin sulphate (60HMs) (μmol/4 h) ($N = 6$, patient IV with β-blocker) and urinary cortisol (CS) (nmol/4 h) ($N = 7$) measured at five intervals/day over 48 h. The urine samples were collected before, on day 4 and 5 of light and 9–10 of light, and after cessation of light administration. Both hormones showed a circadian rhythm by ANOVA: (60HMs $P < 0.0005$; CS $P < 0.01$). There was no difference between day 1 and day 2 of collection, so these were averaged. An interaction between treatment and time of day ($P < 0.03$) in the 60 HMs profiles was analysed for simple effects. This shows a slight increase in total nocturnal 60HMs at the end of the light period ($P < 0.05$)

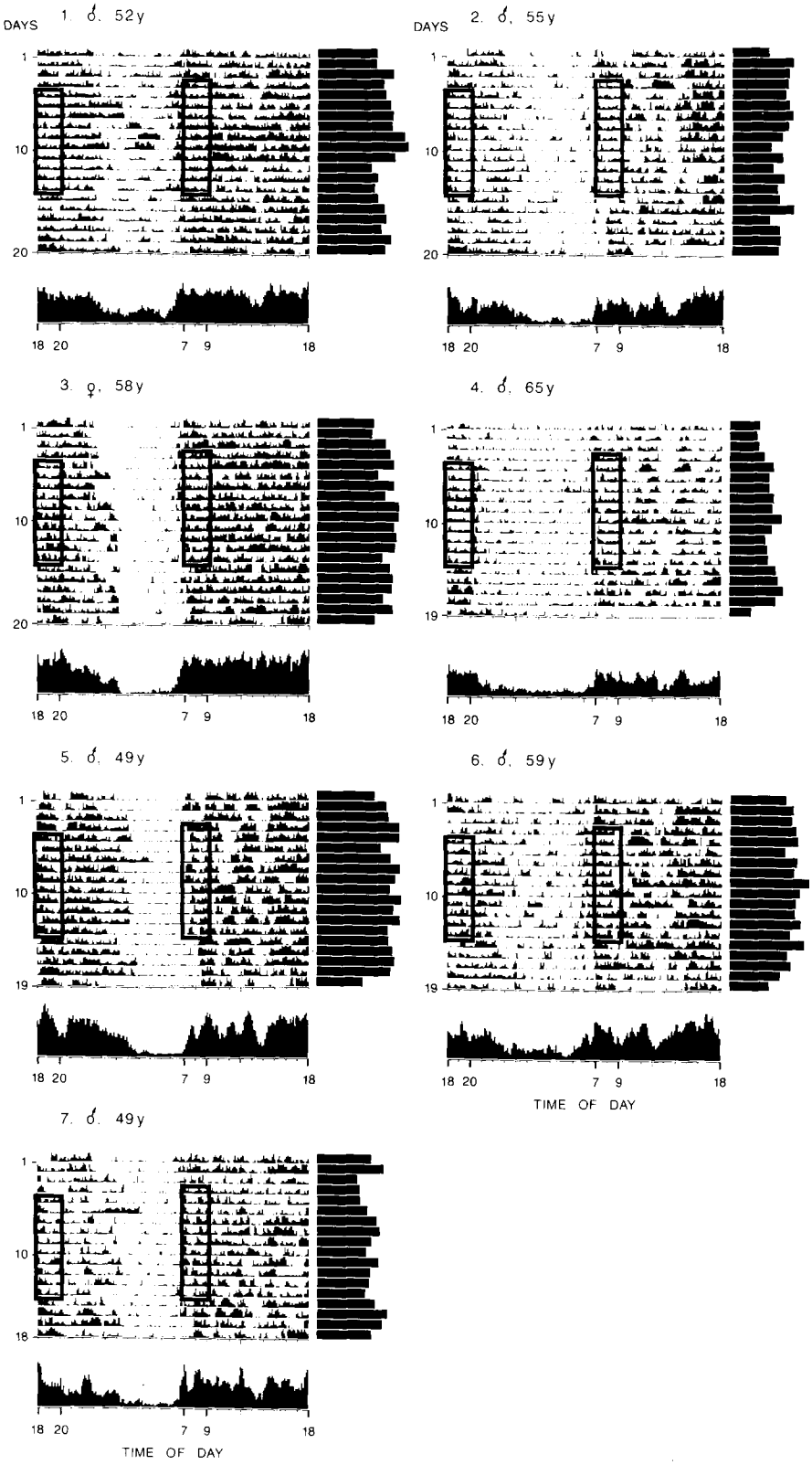

Fig. 4. Wrist-activity measured throughout the protocol at 15-s intervals in each patient. The bouts of rest measured during the day could reflect the narcoleptic attacks. The activity bouts during the night indicate the disturbed sleep. The restactivity pattern does not change during the light administration *(marked areas)*. The *filled bars* at the right side of each chart represent the 24 h total motor activity. The *filled area* on the bottom is an average over the entire study of an individual's circadian pattern of activity and rest

continuously throughout the entire period by means of an actometer worn on the non-dominant wrist [5]. Self-ratings of tiredness, mood and anxiety (visual analogue scales) were carried out in mornings and evenings, together with a sleep and cataplexy log book. Urine samples collected at five intervals per days over 48 h were used for measurement of free cortisol [6] and 6-hydroxy-melatonin sulfate (60HMs) [1].

Results

Light therapy had neither objectively measurable nor subjectively experienced effects on the clinical symptoms of narcolepsy. There was no change in self-ratings of mood, anxiety or tiredness (Fig. 2).

The only modification of the sleep EEG was a significant increase of NREM stage II (t test, $P < 0.01$), and an improved sleep efficiency ($P < 0.05$). Daytime vigilance, as measured by the MSLT and signal reaction test did not improve with light. The individual rest-activity cycles throughout the entire experimental protocol are shown in Fig. 4. They document the characteristic pathological fragmented pattern of daytime activity in narcolepsy, not modified by the exposure to bright white light.

The circadian rhythms of cortisol and 60HMs were normal, the former with maximal excretion in the morning, the latter peaking in the overnight sample (Fig. 3). No phase shift could be seen in these urinary rhythms after light treatment, although the same timing of light has been shown to advance plasma melatonin by 1–2 h [16, 22]. If a similar magnitude shift had occurred, it was probably too small to be evident in four 8-h urine sampling aliquots. Total nocturnal melatonin excretion was slightly increased after 9–10 days of light ($P < 0.05$).

Discussion

Bright light had no effect on any of the symptoms of narcolepsy. The slight improvement in sleep profiles at the end of light treatment were not correlated with consolidation of the fragmented sleep architecture or augmentation of deep sleep. Diurnal vigilance remained low.

The "dosage" light used was of an intensity and duration known to phase shift circadian rhythms in man [13, 16, 22] and improve depression and hypersomnia in patients with seasonal affective disorder [16, 23, 27, 28]. A type II error, too little light for too short a time, is not excluded from this study. However, since we were considering bright light as a potential therapeutic agent for narcolepsy, more than 4 h light exposure per day is unrealistic.

Although a negative therapeutic finding, the theoretical implications are important. Narcoleptic patients contrast with patients with seasonal affective disorder, who show marked and rapid improvement of symptoms under a similar protocol. This distinction speaks against only a placebo effect of light therapy in the seasonal disorder.

Our group of narcoleptic patients had normal circadian rhythms of cortisol and 60HMs. The lack of disturbed circadian rhythmicity indicates that this sleep disorder is not related to process "C". The available literature supports this conclusion [3, 19, 24]. Since bright light acts directly on the circadian pacemaker, the lack of response of narcoleptic symptoms provides still further evidence for such an interpretation.

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