# Light Treatment for Sleep Disorders: Consensus Report.

## IV. Sleep Phase and Duration Disturbances

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*Abstract* Advanced and delayed sleep phase disorders, and the hypersomnia that can accompany winter depression, have been treated successfully by appropriately timed artificial bright light exposure. Under entrainment to the 24-h day-night cycle, the sleep-wake pattern may assume various phase relationships to the circadian pacemaker, as indexed, for example, by abnormally long or short intervals between the onset of melatonin production or the core body temperature minimum and wake-up time. Advanced and delayed sleep phase syndromes and non-24-h sleep-wake syndrome have been variously ascribed to abnormal intrinsic circadian periodicity, deficiency of the entrainment mechanism, or—most simply—patterns of daily light exposure insufficient for adequate phase resetting. The timing of sleep is influenced by underlying circadian phase, but psychosocial constraints also play a major role. Exposure to light early or late in the subjective night has been used therapeutically to produce corrective phase delays or advances, respectively, in both the sleep pattern and circadian rhythms. Supplemental light exposure in fall and winter can reduce the hypersomnia of winter depression, although the therapeutic effect may be less dependent on timing.

*Key words* sleep, circadian rhythms, light, phototherapy, delayed sleep phase syndrome, advanced sleep phase syndrome, non-24-h sleep-wake syndrome, hypersomnia, seasonal affective disorder

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## INTRODUCTION

Several sleep phase and duration disorders are responsive to daily administration of artificial light of appropriate intensity, duration, and time of presentation. Sleep phase disorders include delayed sleep phase syndrome (DSPS; ICSD 780.55-0; American Sleep Disorders Association, 1990), sleep onset insomnia with normal awakening, advanced sleep phase syndrome (ASPS; 780.55-0), early-morning awakening with normal sleep onset, and non-24-h sleep-wake syndrome (780-55.2). Duration disorders include the hypersomnia that can accompany seasonal affective disorder (SAD) in fall and winter (DSM-IV 296.3 to 296.7, or 296.89; American Psychiatric Association, 1994). Increased sleep length is usually specified as a change for a given individual ("relative" hypersomnia), and may fall within the normal range. Such sleep patterns may bear similarity to idiopathic hypersomnia (ICSD 780.54-7) and long sleeper disorder (ICSD 307.49-2), but the diagnostic matches are inexact. A second light-responsive duration disorder is hyposomnia, usually accompanied by advanced sleep phase, which has been studied mainly in the elderly and is the focus of a separate section of this task force report (Campbell et al., 1995b [this issue]).

## DELAYED AND ADVANCED SLEEP PHASE SYNDROMES

### Description of the Syndromes and Circadian Rhythm Correlates

ASPS is characterized by early sleep onset and early morning awakening. Patients experience difficulty staying awake in the evening and maintaining sleep past a predawn hour (e.g., 0300 h). DSPS is characterized by difficulty in initiating sleep before 0100 to 0300 h, sometimes later. Once sleep is initiated, patients have no difficulty maintaining it for a normal duration. Patients with DSPS often evolve work and social schedules with late morning starts and intense nighttime activity. Strictly speaking, the sleep phase disorders are present only when voluntary efforts to normalize sleep phase fail; many adolescents, for example, adopt abnormally late sleep schedules but can readjust at will. Whether or not the sleep pattern is subject to self-control, however, appropriate lighting interventions can serve to guide such sleep into a normal phase. Although DSPS predominates at younger age and ASPS at older age (see related task force section, Campbell et al., 1995b), the syndromes may be chronic and can present difficulty throughout one's life, including occupational and marital risks. It has been commonly assumed that sleep duration and architecture are normal in the sleep phase syndromes and that the sleep episode retains a normal phase angle with respect to the delayed or advanced internal clock phase. Early studies of DSPS (Czeisler et al., 1981; Weitzman et al., 1981) found no consistent abnormalities in the polysomnogram (PSG) except for delayed sleep onset. Similarly, Alvarez et al. (1992) and Okawa et al. (1993) found normal sleep architecture. Data concerning circadian phase vary. In a case report of ASPS (Singer and Lewy, 1989), nocturnal melatonin secretion phase was found to be within the normal range; however, a group of early morning insomniacs showed phase advances in the core body temperature minimum (mean $T_{min}$ at 0231 h) measured under a constant routine (Lack and Wright, 1993). Major delays in $T_{min}$ have been found in DSPS (e.g., 0830 to 1230 h; Okawa et al., 1993), and a group of sleep onset insomniacs were delayed relative to controls (0718 h vs. 0315 h; Morris et al., 1990). Although sleep duration in DSPS has appeared normal according to clinical observation by many groups (e.g., Shirakawa et al., 1993), a comparison with controls revealed an average hypersomnic pattern (approximately +1 h); specifically, the interval between $T_{min}$ and the time of awakening was lengthened (Okawa et al., 1994).

To judge by available data, it appears that the initial or terminal insomnia seen in the sleep phase disorders is often associated with altered circadian timing (ASPS and early morning awakening showing advances, and DSPS and sleep onset insomnia showing delays). Considering that the phase angle of entrainment is known to depend on the intrinsic circadian period (cf. Pittendrigh and Daan, 1976), one might predict abnormally long periods for DSPS patients tested under free-running conditions, and short periods for ASPS patients. Although free-running data are lacking, such an explanation of displaced sleep phase under entrainment is plausible based on temporal isolation studies of elderly subjects, an age group vulnerable to ASPS, who showed short free-running periods (Weitzman et al., 1981; Czeisler et al., 1986). An alternate circadian explanation for DSPS—yet to be tested—is a reduced capacity for circadian phase advances, as would result from a diminished phase-advance portion of the phase response curve (PRC) (Czeisler et al., 1981; Weitzman et al., 1981). Even with a normal PRC, however, DSPS patients might miss the opportunity for a

corrective phase advance due to extended sleep after $T_{min}$ (Okawa et al., 1994)

In addition to the factor of delayed or advanced phase relative to external clock time, the sleep phase disorders are often characterized by variations in the internal phase angle between the circadian pacemaker and the sleep episode. Lewy (1990a) has posited three distinct classes of phase-angle relationship: (a) normal (e.g., with 10-h separation between the onset of nocturnal melatonin production and final awakening), (b) sleep delayed relative to the internal clock (e.g., 13-h separation), and (c) sleep advanced relative to the internal clock (e.g., 7-h separation). An example of the third type is seen in the comparison of sleep onset insomniacs and normal controls by Morris et al. (1990): insomniacs slept more than 2 h earlier relative to $T_{min}$, even though $T_{min}$ fell 4 h later than normal in external clock time. In an analysis of such internal phase relationships, Strogatz et al. (1987) identified regions of the temperature cycle during which spontaneous sleep onset rarely occurred during free-runs in temporal isolation. Thus, under 24-h day-night cycles, if sleep is attempted during the evening wake-maintenance zone, sleep onset insomnia would result.

The loose association between sleep timing and circadian phase implies the contribution of noncircadian factors to the abnormal patterns. Sleep onset and awakening are themselves to some extent under volitional control (e.g., guided by schedule commitments) and can deviate from times predicted by circadian sleep-wake thresholds (Daan et al., 1984). DSPS patients also frequently show psychosocial adjustment problems or personality disorders, which might interact with the choice of sleep timing. Another vulnerable group is shift workers, who may develop DSPS following shift rotations (Guilleminault et al., 1982).

### Therapeutic Interventions with Light

A historical antecedent to light treatment for DSPS was chronotherapy, in which the timing of sleep was gradually shifted later in 3-h daily steps for about 1 wk, until the desired target phase was reached (Czeisler et al., 1981). The shift procedure was based on the observation of free-running periods > 24 h in temporal isolation studies (e.g., Aschoff, 1965; see also related task force section,Dijk et al., 1995 [this issue]). The objective was to reset the phase of the circadian pacemaker, which would then regulate the timing of sleep at an earlier hour. Following chronotherapy, it has sometimes been possible to maintain the target phase for weeks or months. In a case report, ASPS was similarly treated by successive phase advances of sleep (Moldofsky et al., 1986). Although the method does not explicitly manipulate light exposure, by shifting the sleep schedule, patients might be exposed to light at times of day (morning for DSPS, evening for ASPS) that would maintain entrainment at the normalized phase position. The chronotherapy procedure is arduous and requires reserving about a week's time for sleeping during daylight hours as the progression moves around the clock; home treatment may be difficult because of competing environmental cues not conducive to daytime sleep. Although chronotherapy may succeed in resetting both circadian and sleep phases, maintenance of the effect has been difficult (cf. Ohta et al., 1992). Further, there is a risk of relapse if the target sleep schedule is not strictly maintained. Explicit light treatment presents an alternate strategy.

The development of bright light treatment for sleep phase disorders was prompted by the finding that such light is more effective than low-intensity indoor light for suppressing nocturnal melatonin production (Lewy et al., 1980). It was demonstrated that the range of entrainment of the temperature and activity-rest rhythms was greater using a bright light/dark cycle than ordinary room light (Wever et al., 1983). In a more analytical approach based on the assumed characteristics of the PRC for light, exposure was confined to the morning or to the evening in order to advance or delay circadian rhythms, respectively. Lewy et al. (1987) demonstrated selective phase-shifting effects of morning and evening bright light on the onset of nocturnal melatonin production (dim light melatonin onset [DLMO]), while sleep-wake cycles were held constant. Similarly, Czeisler et al. (1986) demonstrated that evening light produced a large phase delay of $T_{min}$, as assessed under constant routines, in a subject who showed an intrinsic period of 23.7 h under forced desynchrony (see also related task force section, Dijk et al., 1995).

Lewy et al. (1985) proposed that appropriately timed bright light exposure can alleviate DSPS and ASPS. They described a patient with DSPS for whom daily advances of light exposure at about 2500 lux for 1 h upon awakening served to normalize sleep phase in 3 to 4 days. Two case studies by Czeisler et al. (1988) demonstrated that 3 days of light exposure at about 10,000 lux for 4 to 5 h resulted in a phase advance of $T_{min}$ of 3 h in a patient with DSPS (exposure upon awakening), and a phase delay of 2 h in a patient with

ASPS (exposure before sleep). Both patients showed appropriate adjustments in their sleep-wake pattern. Similarly, maintenance treatment with evening light (2 h at 2500 lux) in an ASPS patient resulted in a phase delay of the DLMO as well as the sleep-wake pattern (Singer and Lewy, 1989). Relatively few studies of ASPS have been performed (cf. related task force section, Campbell et al., 1995b), although by now many DSPS patients have been treated (e.g., Rosenthal et al., 1990; Terman, 1993a). By exposing DSPS patients to light of 2500 lux for 2 h between 0600 h and 0900 h, $T_{min}$ was advanced by > 1 h relative to a 300-lux control (Rosenthal et al., 1990). Although they did not measure the accompanying advance of sleep onset and offset, patients reported improved sleep, and the tendency to quickly fall asleep decreased in multiple sleep latency tests early in the day. Lack and Wright (1993) reported a delaying effect of evening light in a group of patients with early morning awakening but normal sleep onset. After two nights of 2500-lux light exposure at 2000 h to 2400 h, $T_{min}$ delayed from 0231 h to 0422 h, while the DLMO delayed from 2113 h to 2327 h. In addition, morning awakening was delayed by about 1 h, with a similar increase in sleep duration, and no change in sleep onset time.

For patients with DSPS, exposure to light is usually scheduled immediately upon awakening. At the start of treatment, DSPS patients often undergo a very unpleasant period of sleep deprivation. They continue to have difficulty falling asleep, while they are required to awaken for morning treatment. Although research studies have typically used a constant early-morning treatment time (e.g., 0600 h to 0800 h), for practical clinical application it is often wise to advance the treatment time in gradual steps (e.g., 10 to 30 min) toward the targeted hour. If sleep is truncated during this period of adjustment, the patient may require reassurance that a normal duration will be recaptured.

In a study of ASPS in elderly patients, Campbell et al. (1993) applied light of 4000 lux for 2 h between 2000 and 2300 h, which served to delay $T_{min}$ by more than 3 h and to increase sleep efficiency and Stage 2, rapid eye movement (REM), and slow wave sleep. As a general clinical strategy in ASPS, sleep onset may be gradually delayed, with exposure to light 2 to 4 h before scheduled bedtime. Sometimes these patients complain of an energizing effect of light causing sleep onset insomnia, in which case light exposure is scheduled to end at least 1 to 2 h before scheduled bedtime (see related task force section, Campbell et al., 1995a [this issue]).

Parameters of light exposure have varied widely, from 15 min to 4 h using illuminance levels from 2500 to 10,000 lux from fluorescent sources. Once the target phase has been achieved, some patients are able to reduce the duration of light exposures, or skip days occasionally, without slipping back toward their delayed sleep phase. For a given exposure duration, increased light intensity within the therapeutic range may result in increased phase shifts (cf. Lack and Wright, 1993). Exposure to sunlight also can be effective (Dagan et al., 1991), assuming that the time of awakening is after natural dawn. In addition, chronotherapy for DSPS has been reinforced with explicit morning bright light exposure at the target phase (Eastman et al., 1988; Terman, 1993a), including walks outdoors upon awakening.

Scheduling of light treatment for DSPS has usually been made without baseline assessments of circadian phase (as by core body temperature measurement or melatonin assay), but has been based on the sleep pattern itself. Given that sleep can occur out of phase with the circadian subjective night, there is a risk of obtaining exaggerated phase shifts, or even phase shifts opposite in direction to that predicted for light exposure at a specific time of day. In one such case, a patient scheduled for 30 min, 10,000-lux light exposure at 0715 h began awakening prematurely at about 0500 h (Terman, 1993a), but normalized with reduced exposure duration. In another case, a patient began treatment with 2500-lux, 2-h exposures at 0600 h, rather than advancing gradually. Not only did the sleep interval fail to advance, but melatonin showed a phase delay, which could have resulted from stimulation of the delay portion of the PRC if the delay-to-advance crossover point were itself markedly delayed (A. J. Lewy and R. L. Sack, personal communication, 1994). Since circadian temperature and melatonin markers are not readily available in clinical practice, the clinician must closely monitor the progress of sleep phase adjustment for several weeks upon initiation of treatment in order to avoid undesired responses.

Although light treatment is simple in concept, in practice case management is often complicated (for a discussion of dosing and scheduling strategies, see Terman, 1993a). Many of these individuals have adjusted to a pattern of delayed sleep phase and are reluctant to shift earlier. Despite high success rates for achieving the shift under acute treatment, a majority of patients subsequently fail to comply with the recommended light schedule and allow themselves to relapse. Some are able to maintain a normalized sleep

phase without treatment for periods of up to several months, while others drift back toward the delayed sleep phase within days. Some reestablish the advanced phase by periodic light treatment, in response to social or occupational demands.

Compliance with early morning light treatment, and success of the procedure, might be improved by automatic presentation of the lights in the bedroom toward the end of the scheduled sleep episode. Two such approaches hold promise. In a report by Jacobsen (1990), oversleepers presented with 500-lux light—switched on automatically 10 min before their preselected wake-up time—showed earlier rising and decreased sleep duration. In an attempt to simulate spring and summer sunrises in the bedroom, Terman developed a device that presents a gradually increasing naturalistic dawn signal at the bedside, and patients with winter depression showed improved mood accompanied by earlier rising (Terman et al., 1989; Terman and Schlager, 1990). Dawn simulation has the potential advantage of avoiding the shocking effect of sudden bright light onset during sleep; however, even a dim dawn signal can result in premature awakening if the intensity ramp is too rapid or occurs too early (Avery et al., 1992, 1993). The efficacy of dawn simulation specifically for treatment of DSPS remains to be tested.

## NON-24-HOUR SLEEP-WAKE SYNDROME

Yet another type of sleep-wake disorder results from progressive phase delays of sleep onset and awakening relative to the 24-h day, even when living in normal social environments (Elliot et al., 1971; Miles et al., 1977). Kokkoris et al. (1978) coined the term "hypernychthemeral" to describe such patterns. In the case they described, the period of the rectal temperature rhythm was 24.8 h, and there were variable daily delays of the sleep-wake cycle such that the two rhythms moved in and out of phase with one another. During periods when sleep and temperature were desynchronized the patient reported insomnia, fatigue, and impaired functioning. The authors hypothesized that hypernychthemeral cycles result either from a reduced capacity for entrainment or weakened response to social zeitgebers (as would be consistent with the patient's personality disorder). Noting that some DSPS patients occasionally break into a transient hypernychthemeral pattern, Weitzman et al. (1981) reasoned that non-24-h sleep-wake syndrome and DSPS are associated disorders of varying severity.

In a recent case report, the intrinsic circadian period of a patient with non-24-h sleep phase syndrome was evaluated under a constant routine before and after a forced desynchrony protocol in which sleep was scheduled every 28 h (Emens et al., 1994). Although the baseline sleep-wake period was 25.17 h—similar to that found in normal subjects under temporal isolation—the intrinsic period of the core body temperature rhythm was found to be only 24.5 h. It was suggested that the shifting sleep resulted from the patient's self-selected pattern of light-dark exposure, such that sleep extended through the phase-advance portion of the PRC, facilitating phase delays. This case suggests that non-24-h sleep-wake syndrome may result from inappropriate photic exposure, rather than from an abnormally long intrinsic circadian period or weakened entrainment mechanism. However, in earlier work under temporal isolation, in which two patients with non-24-h sleep-wake disorder showed free-running temperature rhythms with periods of 25.6 h and 25.9 h (toward the long end of the normal range), Honma et al. (1988) were unable to achieve phase advances or entrainment using 5000-lux illumination for 3 or 6 h, administered 1 h after awakening or on a 24-h schedule. They ascribed these failures to reduced light sensitivity of the circadian clock. Positive treatment results have been obtained in two case studies in which hypernychthemeral patterns were halted or greatly decelerated with bright light administered immediately upon awakening (Eastman et al., 1988; Hoban et al., 1989).

The covariation of sleep cycles with circadian rhythms in the blind provides an added perspective. Many blind subjects show free-running rhythms despite adherence to 24-h work and sleep-wake schedules (Lewy and Newsome 1983; Sack et al., 1992). Some, however, show periodic insomnia and daytime sleepiness when core body temperature and other rhythms drift away from the normal nocturnal phase (e.g., Klein et al., 1993). Indeed, sleep propensity—as measured by a multiple napping protocol (Lavie, 1986)—may free-run with other rhythms even though the patient is able to maintain a normal sleep-wake schedule (Nakagawa et al., 1992). However, non-24-h sleep-wake syndrome in the blind is apparently rare (but see Arendt et al., 1988). Okawa et al. (1987) identified four retarded blind children with hypernychthemeral patterns; a light treatment trial failed in a patient with 24.8-h periodicity, but electroretinogram re-

sponse and visual evoked potentials were absent. The recent demonstrations of melatonin suppression (Czeisler et al., 1995) and pupillary contraction (Sack et al., 1992) to light in blind patients without conscious visual perception suggests that the residual retinal function may be sufficient for entrainment of circadian rhythms and treatment of sleep phase disorders with bright light.

The possibility that vitamin $B_{12}$ (methylcobalamin) can forestall non-24-h sleep-wake cycling has recently received much attention, based on an early report by Kamgar-Parsi et al. (1983). Studies by Okawa and associates (e.g., Okawa et al., 1993) indicate that either the vitamin alone, or in combination with morning bright light exposure, can be used effectively to treat this syndrome as well as DSPS. However, a multicenter study showed no advantage of the vitamin over placebo (Takahashi et al., 1994). Honma et al. (1992) has proposed that vitamin $B_{12}$ serves to increase light sensitivity, based on their finding of increased melatonin suppression and enhanced phase advances of the melatonin rhythm in a group of healthy subjects. Additionally, a patient with non-24-h sleep-wake syndrome (period length, 25.9 h) showed distinct subsensitivity to light by similar measures.

## EXOGENOUS MELATONIN ADMINISTRATION AND LIGHT

There have been several reports of the effectiveness of exogenous melatonin in alleviating sleep disturbances in blind patients. For example, in two cases of non-24-h sleep-wake syndrome, 5 mg of oral melatonin successfully synchronized the sleep-wake cycle to a nocturnal phase, with apparent phase shifts in the endogenous rhythms of melatonin production or core body temperature (drug given at 1700 h, Arendt et al., 1988; drug given at 2000 h, Tomoda et al., 1994). In a similar case, a nocturnal dose of 20 mg also served to regularize the sleep pattern, although endogenous melatonin and cortisol rhythms were unaffected (Folkard et al., 1990). Clear cases of re- entrainment associated with sleep improvement have been reported in retarded blind children at a dose of 0.5 mg, given at 1800 h to a 9-yr-old boy (Palm et al., 1991) and at 1930 h to a 5-yr-old girl (Lapierre et al., 1993). Most such studies do not resolve whether the improvement in sleep timing is mediated by circadian or hypnotic actions of the drug. Indeed, sleep has been potentiated by exogenous melatonin administered at times of day that do not foster circadian phase shifts (Dawson et al., 1992).

Sack et al. (1991) were able to show that 5 mg melatonin given at bedtime induced phase advances in endogenous melatonin production in five free-running blind patients, three of whom also showed concurrent phase advances in the cortisol rhythm. A sixth patient showed apparent entrainment of the melatonin rhythm for about a year, using 7 mg doses at 2100 h. The analysis was strengthened by the derivation of a PRC for exogenous melatonin using a group of sighted subjects without sleep disturbance (Lewy et al., 1992). Doses of 0.5 mg in the afternoon or early evening advanced the onset of melatonin production, while morning doses delayed the rhythm. The melatonin PRC thus provides a potential guide for the timing of exogenous melatonin in the treatment of circadian phase disorders, including the sleep phase syndromes. In the first such study, daily 5 mg doses at 2200 h succeeded in phase advancing the sleep episode in patients with DSPS (Dahlitz et al., 1991). This result was confirmed and extended in a similar study that used 5 mg doses at 1930 h (2 h before bedtime), with continued improvement at 6 mo follow-up (Tzischinsky et al., 1993).

Although oral melatonin has been used successfully as a hypnotic agent throughout a wide dosage range (Dollins et al., 1994), results across studies have been variable (for review, see Dawson and Encel, 1993). Delayed sleep phase may thus be responsive to combined circadian and hypnotic effects of the drug administered at or before bedtime, especially at relatively high, pharmacological doses (e.g., 5 mg). For treatment of ASPS with morning melatonin, however, low, physiological doses (e.g., 0.5 mg) may be preferable, given that they are sufficient to elicit phase shifts without hypnotic effect.

A potential interaction between light and melatonin administration seems likely given that the two PRCs bear an opposite phase relationship. Thus morning light elicits phase advances while morning melatonin administration elicits phase delays. Indeed, the melatonin PRC shows formal similarity to the dark-pulse PRC of hamsters (Boulos and Rusak, 1982) and may reflect a similar mechanism of action. The ambient lighting environment is a factor likely to modulate therapeutic response to exogenous melatonin administration, especially at the dawn and dusk transitions when both PRCs are active (Lewy et al., 1995). Thus it may be important for patients to remain under minimal illumination after ingesting the drug at these

hours, in order to avoid an opponent interaction. That said, however, a promising avenue for clinical research is the combined use of exogenous melatonin and bright light at antiphase (morning light/evening melatonin and vice versa), which may serve to expedite and stabilize desired phase shifts of circadian rhythms and sleep.

## HYPERSOMNIA OF SEASONAL AFFECTIVE DISORDER

### Description of the Syndrome

Beyond the cardinal characteristic of mood reactivity—that is, the ability to respond temporarily to positive external events—hypersomnia is one of the defining symptoms of atypical depression (Liebowitz et al., 1984). By contrast, sleep onset insomnia and early morning awakening typify melancholic depression. Although hypersomnia can be observed clinically without seasonal pattern, it often appears specifically in fall and winter at northerly latitudes, in association with seasonal affective disorder (SAD) (Rosenthal et al., 1984). Indeed, more than 90% of patients with SAD fulfill DSM-IV criteria for depressive disorder with atypical features (Terman and Stewart, 1993). About 80% of winter depressives report increased sleep duration, though the symptom is not strongly correlated with other symptoms of SAD (such as carbohydrate craving). Indeed, reports of wintertime hypersomnia (sleep duration at least 1 h longer than in spring or summer) without accompanying depression are common in the general population (Terman, 1988; Anderson et al., 1994). Sleep log studies of SAD patients suggest that retrospective reports of winter hypersomnia are often exaggerated (Anderson et al., 1994). PSG studies have found only marginal increases in sleep duration in SAD patients relative to normal controls (Anderson et al., 1994) and either similar (Endo, 1993; Anderson et al., 1994) or shorter (Kohsaka et al., 1994) sleep durations following light treatment. There are many individual cases showing significant reductions under treatment (cf. Terman, 1993a). Seasonal sleep change is sometimes better described as reduced sleep duration during spring and summer—a symptom of hypomania—than hypersomnia during fall and winter. Some patients show extreme variation in both seasons, for example, $< 6$ h sleep in summer and $> 11$ h in winter.

The most comprehensive studies of sleep architecture in SAD have been performed over the past decade at the National Institute of Mental Health, and summarized by Anderson et al. (1994): "Nocturnal EEG recordings of depressed SAD patients in winter showed decreased sleep efficiency, decreased delta sleep percentage, and increased REM density (but normal REM latency) in comparison with recordings: (1) from themselves in summer; (2) from themselves after $\geq 9$ days of light treatment; or (3) from age- and gender-matched healthy controls" (p 323). Similarly, Putilov et al. (1993) reported decreased slow wave sleep and increased REM percentage during winter while patients were depressed, and increased slow wave sleep after light treatment. By contrast, although Kohsaka et al. (1994) found improved sleep efficiency after light treatment, slow wave percentage did not change. In a comparison of depressed patients with and without seasonal variation, Thase (1989) found the seasonal group to show longer sleep latency and reduced sleep efficiency, but similar percentages of delta, REM density, minutes of REM, and number of awakenings. Similarly, for patients with SAD, Brunner et al. (1993b) found sleep latency and efficiency to improve after light treatment, without change in other parameters. Partonen et al. (1993), however, found no changes at all, despite obtaining positive clinical response to light.

Whether or not a patient is objectively verified as hypersomnic, many report an increased sleep need, that is, that they would sleep longer if their schedule permitted. Such self-imposed limitation on sleep duration—which is confirmed by significantly longer weekend sleep (Anderson et al., 1994)—may contribute to the nearly universal complaint of daytime fatigability. However, many SAD patients with long sleep durations still complain of fatigue. The common symptom of difficulty awakening—which could be associated with self-imposed sleep deprivation—is not correlated with complaints of hypersomnia, although it is correlated with severity of depression (Avery et al., 1994). Even so, several studies have found the symptom of hypersomnia to be a predictor of clinical response to light treatment (Avery et al., 1991; Lam et al., 1992; Oren et al., 1992; Terman, 1993b).

Some SAD patients show DSPS specifically in the fall and winter (e.g., Endo et al., 1992), which is not necessarily accompanied by hypersomnia. Sleep specialists who encounter complaints of DSPS during these months are advised to screen for associated depressive and atypical neurovegetative symptoms and not to treat the sleep disorder in isolation. Seasonal

recurrence of DSPS may, however, occur without depression (Uruha et al., 1990).

## Role of Circadian and Sleep Processes in Hypersomnia

The origin of hypersomnia is not yet understood but may be related to circadian phase. An early study found relatively long sleep episodes to occur when sleep was initiated at a phase of high core body temperature, while shorter episodes were found with sleep onsets near $T_{min}$ (Czeisler et al., 1980). Cases of extreme circadian phase delay—with the onset of melatonin production after midnight—have been noted in winter depressives (e.g., Terman et al., 1988). If a patient maintains a normal bedtime, with sleep onset earlier relative to a delayed core body temperature rhythm, hypersomnia could result given the association of spontaneous awakening with the morning rise in temperature (Zulley et al., 1981).

An expanded, complementary account of hypersomnia derives from the two-process model of sleep regulation (Borbély, 1982; Daan et al., 1984), in which sleep timing and duration result from an interaction between distinct homeostatic (S) and circadian (C) processes. Process S reflects sleep debt and is indexed by slow wave (prominently, delta) encephalogram (EEG) activity, which predominates in the early hours of sleep and decays across successive NREM-REM (nonrapid eye movement and rapid eye movement sleep) cycles. Sleep is initiated and terminated when Process S reaches an upper and lower threshold, respectively. Process C consists of a circadian variation in these thresholds, which is generated by a single pacemaker that also drives the rhythms of body temperature and melatonin production.

Theoretically, there is a variety of ways in which changes in Process S and C, or their interaction, could produce hypersomnia. An acceleration of Process S during waking hours would result in an elevated level at sleep onset; if the decay were unaltered during sleep, hypersomnia would result. An experiment performed on recovery sleep in SAD patients who had been sleep-deprived under a constant routine found no differences in EEG power density between winter and summer or before and after light treatment (Brunner et al., 1993a). However, it must be pointed out that these patients did not exhibit winter hypersomnia, and even during baseline sleep, EEG power density was similar across all conditions (Brunner et al., 1993b). Thus it remains possible that patients with hypersomnic baseline sleep would show a contrasting response to sleep deprivation.

In contrast to an acceleration of Process S during waking hours, hypersomnia could also result from a reduced decay rate of Process S during sleep, under which it would take longer to reach the wake-up threshold. By this account, EEG power density in the first part of the night would increase following light treatment. Such change could represent a direct influence of light on Process S, or reflect the compression of slow wave sleep into a normalized sleep interval. Study of a small sample of SAD patients did suggest an increase in the power density of delta activity (Mendelson et al., 1989). Furthermore, a significant enhancement of EEG sleep stages 3 and 4 has been found in the first 3 h of sleep—following light treatment as well as in summer—without a change in REM activity (Endo, 1993). On the one hand, prolonged sleep duration might augment the depletion of Process S, accounting for reduced slow wave sleep while depressed. On the other hand, since delta activity normally reaches a lower plateau after 3 to 4 NREM-REM cycles, extending sleep might not result in further reductions. Rather, reduced slow wave sleep might result from the shorter waking period of hypersomnic patients, which would provide less time for Process S accumulation.

Even if Process S were undisturbed, there are three types of change in Process C that could lead to hypersomnia: phase delay (as discussed above), lowering of the mean level or amplitude, or altered waveform of the lower (wake-up) threshold. The amplitude hypothesis, originally proposed by Czeisler et al. (1987), has not been confirmed in constant-routine measurements of SAD patients (Wirz-Justice et al., 1994). The waveform hypothesis remains viable, given that morning and evening oscillatory components of the pacemaker can vary independently across the seasons (Pittendrigh and Daan, 1976; Illnerová and Vaněček, 1982). The distributions of sleep and melatonin production broaden significantly under artificially imposed long nights in normal subjects (Wehr, 1991), and it remains to be determined if such responses to night length are magnified in SAD.

## Therapeutic Interventions with Light

As mentioned earlier, hypersomnia—with or without delayed sleep phase—is characteristic of some but not all patients with SAD and is also seen as seasonal variation in sleep duration in the general population.

Based on clinical interviews, sleep logs, and actigraphy, patients who show an antidepressant response to light treatment often also show normalized sleep duration. In one study, light treatment served to advance the average time of awakening and to reduce total sleep duration under either morning or evening exposures of 10,000 lux in 30-min sessions (Terman, 1993a). However, when there was no antidepressant response, sleep duration failed to contract even though morning light succeeded in inducing phase advances of sleep and evening light-induced phase delays. An actigraph study also showed reduced sleep duration after 10,000 lux light treatment morning sessions of 30 to 60 min (Teicher et al., 1994), but no correlation with the magnitude of antidepressant response.

The relative contribution of specific effects of light and placebo effects to the global antidepressant response, or to contraction in sleep duration, remains unresolved. Two studies have found that the response to a placebo control—a deactivated negative ion generator—was similar to that for bright light (Eastman et al., 1992, 1993b), which suggests that contraction in sleep duration may accompany improved mood due to nonspecific factors. In another study, however, a similar placebo control—low-density negative ions—yielded clinical improvement in fewer than 20% of cases, which contrasts with about 60% after bright light treatment (Terman and Terman, 1994, 1995).

Exposure parameters for light treatment of winter depression have been similar to those used in the sleep phase disorders, ranging from 30 min to 4 h per day, at illuminance levels of 2500 to 10,000 lux. A trade-off relation between duration and intensity is generally assumed, although this rests on the limited observations that remission rates are roughly equal for 2500-lux, 2-h exposures and 10,000-lux, 30-min exposures, and that 2500-lux, 30-min exposures are less effective (J. S. Terman et al., 1990). That said, however, the results of individual studies vary widely, and indeed there have been several studies that used 2500-lux, 2-h exposures and obtained minimal clinical response (for review, see Terman et al., 1989).

The ocular safety of short- and long-term exposure to artificial light at 10,000 lux has been studied by Gallin et al. (1995) using a structured eye examination. Although there are no definite ocular contraindications for light treatment, patients with corneal or retinal pathology, cataract or narrow-angle or primary open angle glaucoma were excluded as a precaution and for experimental homogeneity. No adverse ocular effects were found after cumulative irradiant doses as high as 40 J/cm$^2$ (corresponding to 1250 h of 10,000-lux exposure over five years). Several mild side effects, such as eye irritation, were noted on initiation of treatment, but these waned quickly or were controlled by dose reductions. Gallin et al. recommend ocular screening of all prospective patients, and a narrowing of definite exclusions to those with progressive retinal disease. Furthermore, although no adverse drug-light ocular interactions have been found, they recommend periodic ophthalmological monitoring of patients taking potentially photosensitizing medications (e.g., tricyclic antidepressants, phenothiazines, and lithium).

The hypothesis of a pathogenic circadian phase delay in SAD, leading to the prediction of superior response to morning over evening light (Lewy et al., 1987; Sack et al., 1990), is only partially confirmed by clinical trials including hundreds of patients. Patients studied in parallel groups (e.g., Wirz-Justice et al., 1993) usually have not shown this time-of-day difference. In crossover studies, however, patients who receive a period of evening light following an initial period of morning light show reduced antidepressant response (for review, see Terman, 1993b). When evening light is given as first treatment, clinical response is superior. Phase delays of the DLMO to evening light are greatly magnified following phase advances to morning light, which may account for the differential evening-light deficit.

The importance of the phase angle difference between sleep and the circadian pacemaker is suggested by a pilot study that directly manipulated the timing of sleep rather than light exposure (Lewy, 1990b). Patients showed clinical improvement when instructed to go to sleep and arise later. It was surmised that the phase angle difference between sleep and the (delayed) circadian pacemaker thus contracted, as might also happen when morning light serves to advance the circadian rhythm relative to sleep. By this view, depressive symptoms and hypersomnia emerge when circadian rhythms drift later relative to sleep, in response to the delayed winter dawn signal (see also Illnerová et al., 1993). However, recent findings of similar circadian phase positions in winter depressives and normal controls (e.g., Eastman et al., 1993a; Wirz-Justice et al., 1993) raise doubts about the importance of phase delays in predicting antidepressant response to light. The phase-shift hypothesis may apply specifically to vulnerable hypersomnic patients (cf. Dahl et al., 1993). One study has shown a positive correlation between clinical improvement and the magnitude of phase advances of the DLMO to morn-

ing light, but no significant correlation with phase delays to evening light—even though light at either time of day yielded similar antidepressant response (Terman and Terman, 1994).

The data do not rule out the possibility that response to evening light is primarily a placebo effect. By this interpretation, once a patient has experienced the specifically active effect of morning light, response to evening light is reduced (J. S. Terman et al., 1990). In clinical practice, most patients have been treated with morning light, but a trial of evening light is recommended if morning light fails (Rosenthal, 1993). Most patients given 30-min treatment sessions prefer morning to evening exposures, and report superior subjective improvement even when evening light is equally effective according to rating scale scores (M. Terman and J. S. Terman, personal communication, 1994).

In summary, hypersomnia in SAD can be effectively treated with bright light. Although the symptom need not be present for light to have an antidepressant effect, the report of hypersomnia is a positive predictor of response. The efficacy of light treatment for nonseasonal hypersomnia, either as a primary sleep disorder or a symptom of atypical depression (cf. Stewart et al., 1990), remains in question.

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