

# Phase-Shifting Effects of Bright Morning Light as Treatment for Delayed Sleep Phase Syndrome

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**Summary:** Bright light has recently been shown to have phase-shifting effects on human circadian rhythms. In this study we applied this effect to 20 patients with delayed sleep phase syndrome (DSPS) who were unable to fall asleep at conventional clock times and had a problem staying alert in the morning. In a controlled treatment study, we found that 2 h of bright light exposure in the morning together with light restriction in the evening successfully phase advanced circadian rhythms of core body temperature and multiple sleep latencies in these patients. This finding corroborates the importance of light for entraining human circadian rhythms. **Key Words:** Circadian rhythms—Light—Temperature—Sleep latencies.

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Although visible light has long known to influence the circadian system in animals and plants, only recently has its importance in entraining circadian rhythms in humans been appreciated. Czeisler et al. first showed that modification of the light-dark cycle could influence the timing of human circadian rhythms (1), but it was initially unclear whether light and dark were acting only indirectly via their effects on sleeping and waking or directly on the circadian pacemaker. Lewy et al. showed that bright light but not ordinary room light is capable of suppressing nocturnal melatonin secretion in humans (2). Similar bright light has subsequently been shown to have antidepressant effects in patients with seasonal affective disorder (winter depression) (3-5) and direct phase-shifting effects in humans (4,6-8).

Such phase-shifting properties have been postulated by some researchers to underlie the therapeutic effects of light in seasonal affective disorder (4) and have been suggested to be of potential value in correcting disordered sleep and biological rhythms, such as occur in jet lag, shift work, and delayed sleep phase syndrome (DSPS) (9-11).

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The DSPS patients suffer from chronic inability to fall asleep and wake up at conventional clock times. In addition, morning sleepiness, with its associated job-related difficulties, is a major complaint.

In this study we have tested the hypothesis that patients with DSPS can have their circadian rhythms successfully phase advanced by a combination of bright environmental light in the morning and light restriction in the late afternoon and evening (12). The rationale for this hypothesis is based on the so-called phase-response curve (PRC) (13). The PRC is a graphic representation of the relationship between time of exposure to a light pulse and direction and magnitude of the resulting shift in circadian rhythm, which is a fundamental property of the circadian system in animals. Recent evidence of such a PRC in primates (13) lends new support to the suggestion framed initially by Lewy et al. (11) and later supported by Czeisler et al. (6,7) that such a PRC occurs in humans as well (4,8). Specifically, exposure to light early in the subjective night phase delays rhythms, while exposure to light late in the subjective night phase advances rhythms. Exposure to light during the subjective day seems to have little or no effect on circadian rhythms.

## METHODS

We recruited patients via advertisements in the local media, screened them clinically, and admitted those who met a modified version of the DSPS criteria of Weitzman et al. (14). These modified criteria, based on the results of a demographic study of 400 respondents, were: (a) sleep onset after 1:00 a.m. at least 4 nights a week for at least 3 years, (b) significant disruption of work or personal relationships due to sleep patterns, and (c) inability to be alert in the morning (especially between 7:00 and 9:00 a.m.).

Diagnoses were corroborated by a month of sleep log ratings and wrist-worn activity monitoring. Electroencephalographically recorded sleep studies and psychiatric interviews were administered to exclude other sleep disorders and active psychiatric disturbances, respectively. The polysomnography (PSG) sleep studies were scored according to the methods and criteria of Rechtschaffen and Kales (15). The PSG was used to screen for excessive myoclonus and sleep apnea and for indications of sleep patterns consistent with disruptions produced by depression or substance abuse. The structured clinical interview for DSM III-R (SCID-R) was used to screen out candidates with a current diagnosis of any axis I or II psychiatric disorder that could cause an abnormal sleep pattern.

Ninety people were screened clinically by one of the staff doctors; 33 received SCID-Rs administered by the staff social worker and PSGs were analyzed at Johns Hopkins Sleep Center. Twenty of these patients completed the study protocol. Temperature data were available on 20 of the patients for the "active" condition and 16 for the "control" condition. Multiple sleep latency data were available for 15 of the patients for the "active" condition and 17 for the "control" condition.

We designed the study to be a crossover between an "active" treatment and a "control" treatment. The active treatment consisted of 2,500-lx full-spectrum light treatment for 2 h in the morning between 6:00 and 9:00 a.m. and dark goggles in the evening, worn from 4:00 p.m. until dusk. After dusk, light was restricted to one or two bedside lamps. The control treatment consisted of 300-lx full-spectrum light for 2 h between 6:00 and 9:00 a.m. and clear goggles, worn from 4:00 p.m. until dusk. After

dusk, light was restricted to one or two bedside lamps. Patients were randomly assigned to one of the two treatment conditions to prevent an ordering effect. We controlled the timing of awakening during the study, keeping it constant for each patient within each condition. This was reinforced by having the patients call into our answering machine each morning when they got up to turn on the lights. With the exception of one patient, who due to severity of symptoms could not awaken before 10:00 a.m., all patients adhered to a 6–7:00 a.m. awakening time.

The structure of the two conditions was made to appear as similar as possible to minimize the difference in expectations of outcome between the conditions, thereby diminishing the likelihood that any observed difference would be due to a placebo effect. We tested the a priori expectations before each treatment with a modified version of the questionnaire developed by Borkovec and Nau (16). The four-item questionnaire was given to the patient after a 2-min presentation of each treatment condition. Each patient was treated for 2 weeks and then given a washout period of at least 2 weeks to allow for relapse to occur before crossing over to the alternate treatment condition. If the patient did not relapse from the first treatment after 2 weeks, the second condition was delayed until the patient again met diagnostic criteria. Two patients did not enter the second treatment condition, and their data were not included in our analysis. One of these patients relocated before he had a chance to relapse, and the other did not relapse. Two further subjects refused to comply with experimental conditions and were thus also considered to be dropouts.

Efficacy of treatment was evaluated by subjective reports derived from posttreatment questionnaires, 24-h core body temperature measurements, and multiple sleep latencies. A 12-item posttreatment questionnaire constructed specifically for this study was administered to each patient after completion of the last day of each of the two conditions. To compare patients' self-evaluations of the two treatments, paired *t*-tests were performed on responses to three of the questions: overall efficacy, changes in morning alertness, and sleep times. An analysis of variance (ANOVA) with one repeated measure (condition) and two groups (order) was performed on these three items to investigate a potential ordering effect.

Twenty-four-hour temperature profiles and multiple sleep latency tests were conducted before and after each treatment, in other words, four times for each patient. The core body temperature was measured every 5 min for a 24-h period using a Vitalog monitor and thermistor. The timing of the circadian temperature minima was evaluated by visual inspection by a rater blind to the subject's treatment condition. Temperature data were analyzed in two ways. The ANOVAs with two repeated measures (time and condition) were performed on temperature data at all time points for all subjects in each of the two conditions. Paired *t*-tests were performed on temperature minima. Multiple sleep latency tests were performed both before and after each treatment condition and were scored according to the criteria of Carskadon et al. (17). Results were analyzed by paired *t*-tests for each of the seven time points.

We predicted that patients would show greater improvement from the "active" than from the "control" condition, as measured by both self-reports and circadian rhythm profiles. Specifically, we predicted that the "active" condition would induce greater phase-advancing effects on the circadian rhythm of core body temperature and a selective increase in morning sleep latencies given that drowsiness in the morning is a major symptom of DSPS.

## RESULTS

The results of the expectation questionnaire revealed no significant difference in the patient's expectations of the two treatments, regardless of the order of the treatments ( $F = 2.15$ ,  $df = 1, 11$ ,  $p = 0.17$ ).

Twenty patients completed the crossover study and rated the "active" condition as greatly superior to the "control" condition ( $t = 3.51$ ,  $df = 13$ ,  $p \leq 0.001$ ). Other responses on the questionnaire also favored the "active" treatment. Morning alertness and earlier sleep time were reported to be improved during the "active" condition to a significantly greater degree than during the "control" condition (alertness:  $t = 4.79$ ,  $df = 13$ ,  $p < 0.01$ ; sleep time:  $t = 3.35$ ,  $df = 13$ ,  $p \leq 0.01$ ). There were no significant ordering effects on self-evaluation parameters (overall efficacy:  $F = 0$ ,  $df = 1, 11$ ,  $p = 0.99$ ; alertness:  $F = 0$ ,  $df = 1, 11$ ,  $p = 0.85$ ; sleep time:  $F = 2.01$ ,  $df = 1, 11$ ,  $p = 0.19$ ).

Objective criteria supported the superiority of the "active" condition. Both the pattern of core body temperature and the morning sleep latency values indicated that a significant phase advance in circadian rhythms had occurred in the "active" condition as compared with the "control" condition. Temperature profiles (Fig. 1A and B) revealed a significant phase advance in the sleep-associated part of the temperature rhythm on the "active" condition ( $F = 2.39$ ,  $df = 1, 287$ ,  $p \leq 0.001$ ), whereas no such overall shift was apparent on the "control" condition ( $F = 0.92$ ,  $df = 1, 287$ ,  $p = 0.77$ ). Analysis of the timing of the temperature minima similarly indicated a significantly greater phase advance following the "active" treatment as compared with the "control" treatment. Where the "active" treatment shifted temperature minima by an average of 1 h 25 min ( $t = 2.3$ ,  $df = 18$ ,  $p \leq 0.05$ ), the "control" condition shifted minima by a mere 10 min, which was not significantly different from the baseline ( $t = 0.49$ ,  $df = 15$ ,  $p = 0.63$ ). A significant increase in 9 and 11 a.m. sleep latencies was seen following the "active" condition (Fig. 2A and B; 9:00 a.m.:  $t = 2.44$ ,  $df = 11$ ,  $p \leq 0.05$ , 11:00 a.m.:  $t = 2.75$ ,  $df = 14$ ,  $p \leq 0.05$ ), while there was no change after the "control" condition (9:00 a.m.:  $t = 0.98$ ,  $df = 11$ ,  $p = 0.35$ ; 11:00 a.m.:  $t = 0.35$ ,  $df = 16$ ,  $p = 0.73$ ). There were no significant differences between "active" and "control" conditions at other times of day.

## DISCUSSION

The superior effects of the "active" over the "control" condition suggest that the outcome was specifically related to the modification of the light-dark cycle rather than merely to the nonspecific aspects of the intervention such as waking patients early and engaging them in a research study. The similarity in a priori expectations of the two treatment conditions would argue against a placebo explanation for the superior effect of the "active" condition.

We did not obtain data about the amount and quality of sleep during the treatment weeks, and it is possible that differential amounts of sleep during the different treatment periods might have contributed to the resulting differences in alertness and sleep latencies. One argument against such an explanation, however, would be the selective improvement of alertness and decrease in sleep latency in the morning and not in the evening. Had these changes been the result of differential sleep lengths in the two treatment conditions, one would not have expected such a circadian variation in these parameters.

We conclude therefore that the findings of this controlled study support other evi-

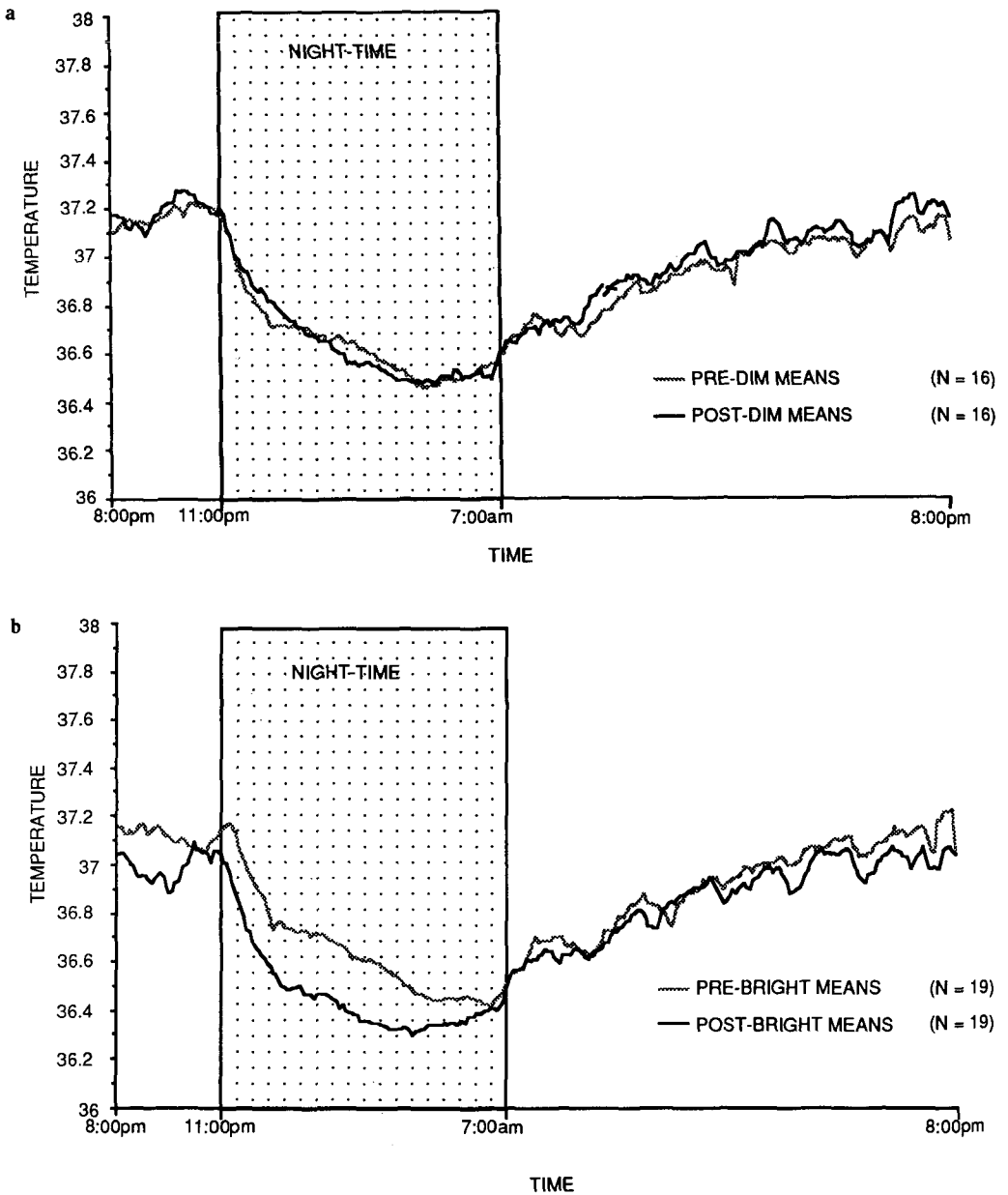


FIG. 1. a: Mean 24-h core body temperature of patients before and after the "control" condition. Core body temperature was measured every 5 min using a Vitalog temperature monitor and a rectal thermistor over the 24-h period. No significant difference in the circadian temperature rhythm was found after the "control" condition ( $F = 0.92$ ,  $df = 1,287$ ,  $p = 0.77$ ). b: Mean 24-h core body temperature of patients before and after the "active" condition. There was a significant difference in the circadian temperature after the "active condition" ( $F = 2.39$ ,  $df = 1,287$ ,  $p \leq 0.001$ ).

dence that modification of timing of light and darkness is capable of exerting a prominent effect on the timing of human circadian rhythms (2,6,7).

Our results would be predicted on the basis of the PRC, the graphic description of the relationship between light exposure and the resulting phase shift in the circadian

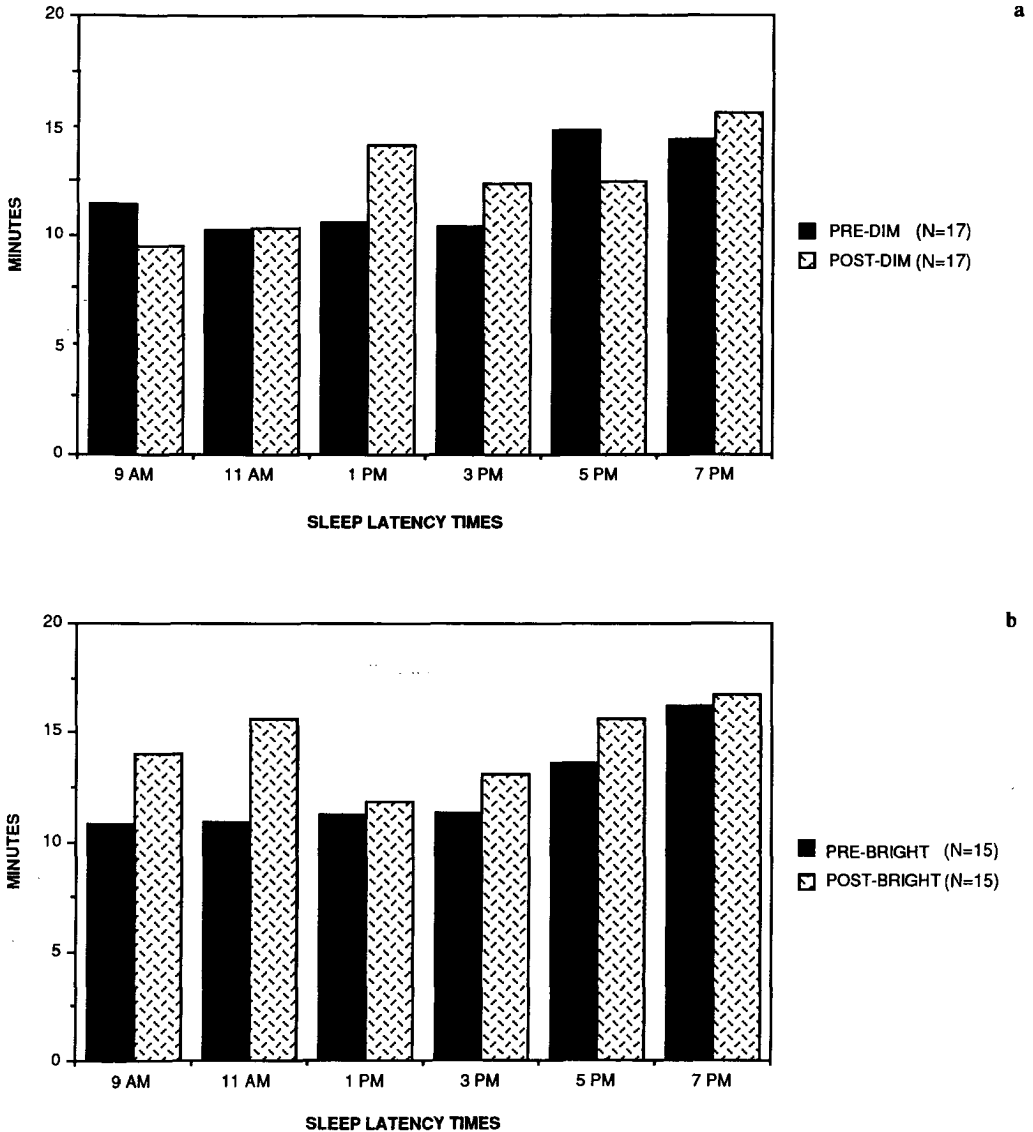


FIG. 2. a: Mean multiple sleep latency times of patients before and after the "control" condition. No significant difference was found at any time point during the day. b: Mean multiple sleep latency times of patients before and after the "active" condition. There was a significant increase in the sleep latency after the "active" condition for 9:00 a.m. ( $t = 2.44$ ,  $df = 11$ ,  $p \leq 0.05$ ) and 11:00 a.m. ( $t = 2.75$ ,  $df = 14$ ,  $p \leq 0.05$ ), just at the times when delayed sleep phase patients report the most drowsiness. There was no significant difference during the other times of the day, when patients tend to be most alert.

rhythms of free-running animals, which is regarded as a fundamental property of the circadian rhythm pacemakers in all animals (11). Our data provide further evidence that such a PRC is present in humans as well. By understanding this PRC, appropriately timed exposure to bright light and darkness can be used to therapeutic advantage in patients with delayed sleep phase syndrome. Other populations, such as shift workers (9) and those suffering from jet lag (8), might also benefit from such treatment.

The improvement in morning alertness generally occurred only in the 2nd week of treatment, a lag that might have been predicted on the basis of other reports on the time required for reentrainment of human circadian rhythms (18). Our subjects reported that they needed to keep using the light to maintain the phase advance of sleeping and waking, which suggests that their circadian rhythms continually tend to drift and need extra assistance in maintaining a normal phase position.

At an average follow-up time of 3 months, 12 patients had purchased fixtures suitable for the administration of bright light and two others were planning to do so. Those suffering from jet lag, however, would presumably need the light only on a temporary basis to reset their rhythms. It is possible that by increasing the intensity of light administered, the morning treatments might be shortened below the 2-h period used in this study. Such an approach has been tried for patients with seasonal affective disorders with promising results (19).

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