Dawn Simulation and Bright Light in the Treatment of SAD: A Controlled Study

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Background: *Some small controlled studies have found that dawn simulation is effective in treating seasonal affective disorder (SAD). With a larger sample size and a longer duration of treatment, we compared dawn simulation with bright light therapy and a placebo condition in patients with SAD.*

Method: *Medication-free patients with SAD were randomly assigned to one of three conditions: bright light therapy (10,000 lux for 30 min, from 6:00 AM to 6:30 AM), dawn simulation (1.5 hour dawn signal from 4:30 AM to 6:00 AM peaking at 250 lux), and a placebo condition, a dim red light (1.5 hour dawn signal from 4:30 AM to 6:00 AM peaking at 0.5 lux.) Over the subsequent 6 weeks, the subjects were blindly rated by a psychiatrist using the Structured Interview Guide for the Hamilton Depression Rating-Seasonal Affective Disorder Version (SIGH-SAD). We modeled the profiles of the remissions (SIGH-SAD ≤ 8) and response (≥50% decrease in SIGH-SAD) to treatment over time using Cox proportional hazards models.*

Results: *The sample consisted of 95 subjects who were randomized to the three conditions: bright light (n = 33), dawn simulation (n = 31) and placebo (n = 31). Dawn simulation was associated with greater remission (p < .05) and response (p < .001) rates compared to the placebo. Bright light did not differ significantly from the placebo. Dawn simulation was associated with greater remission (p < .01) and response (p < .001) rates compared to the bright light therapy. The mean daily hours of sunshine during the week before each visit were associated with a significant increase in likelihood of both remission (p < .001) and response (p < .001).*

Conclusions: *Dawn simulation was associated with greater remission and response rates compared to the placebo and compared to bright light therapy. The hours of sunshine during the week before each assessment were associated with a positive clinical response.* Biol Psychi-
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Introduction

Many controlled studies have found bright light therapy effective in treating seasonal affective disorder SAD (Eastman et al 1998; Lam and Levitt 1999; Terman et al 1989b, 1998; Wesson and Levitt 1998). Although bright light therapy is effective, 69% of SAD patients complain of the inconvenience of finding time to sit in front of the bright light (Oren et al 1991). As many as 19% of SAD patients stop bright light treatment because of inconvenience (Schwartz et al 1996).

Terman et al (1989a) developed dawn simulation, a low intensity light that gradually increases in illuminance before the subject awakens, as a treatment for SAD. Subsequent controlled studies found dawn simulation effective compared to a dimmer control signal. In one study of 22 seasonal affective disorder patients, a 2-hour dawn signal that peaked at 250 lux was superior in efficacy to a placebo dawn that increased over a 30-min period to a peak illuminance of 0.2 lux (Avery et al 1993). In another study of 19 seasonal affective disorder patients, a 1.5 hour, 250 lux dawn signal had greater efficacy compared to a 1.5 hour, 2 lux red signal (Avery et al 1994).

Dawn simulation offers some advantages over traditional bright light box therapy. Because dawn simulation occurs during sleep, it is very convenient. This convenience is likely to result in better compliance than with bright light therapy. The efficacies of bright light therapy and dawn simulation have been directly compared in only two previous trials (Avery et al 1992; Lingjaerde et al 1998). In one study, bright light therapy was superior in efficacy to dawn simulation, but the dawn simulation used in that trial was very bright, 1700 lux, and caused

excessive early morning awakening (Avery et al 1992). In a second study, bright light therapy for 6 days resulted in a superior response compared to 2 weeks of dawn simulation (Lingjaerde et al 1998); however, the final illuminance of the dawn simulation in that study was poorly defined, subjects were allowed to sleep later on weekends, and, after 6 weeks, the responses to the dawn simulation and bright light were similar.

Although bright light therapy has been found effective relative to placebo conditions, most studies of bright light therapy and of dawn stimulation have had a short duration, usually 1 or 2 weeks; only in the last few years have investigators studied bright light therapy in controlled studies lasting as long as 4 weeks. The treatment phase of the present study lasted 6 weeks to determine the persistence of clinical effects of bright light therapy and dawn simulation.

The goals of our study were: (1) To determine whether 6 weeks of dawn simulation is an effective treatment for SAD patients relative to a placebo condition, (2) to determine whether 6 weeks of bright light therapy is an effective treatment for SAD relative to a placebo condition and (3) to determine whether dawn simulation is as effective as bright light therapy in treating SAD.

Methods and Materials

Subjects

SAD patients were recruited through advertisement, referral from physicians, and media exposure over four fall–winter periods. Subjects fulfilled DSM-IV Criteria for Major Depression or Bipolar Disorder, depressed and a fall–winter type of seasonal pattern (American Psychiatric Association 1994). Because hypersomnia is present in the majority of patient with SAD (Rosenthal 1993; Rosenthal et al 1984) and may be relevant to the appropriate timing of light therapy (Avery et al 1990a, 1991), only hypersomnic winter depressives were studied to increase homogeneity. Hypersomnia was defined as sleeping at least an hour more during their winter depression compared to their euthymic summer sleep duration. Subjects who routinely awakened after 9:00 AM were excluded to minimize the possible sleep deprivation imposed by the protocol and to minimize the possibility of the morning light treatments phase delaying rather than phase advancing circadian rhythms; light at 6:00 AM could fall on the phase delay portion of the phase response curve for these patients (Czeisler et al 1989; Minors et al 1991).

We studied patients whose Structured Interview Guide for the Hamilton Depression Rating Scale-Seasonal Affective Disorders Version (SIGH-SAD) (Williams et al 1994) score was $\geq$ 20. The SIGH-SAD is comprised of the 21-item Hamilton Depression Rating Scale (H21) (Hamilton 1967) and eight supplementary items (H8) concerning the atypical symptoms commonly seen in winter depression such as hypersomnia, increased appetite and weight gain. The atypical balance score is defined as 100*H8/ (H21 + H8).

All subjects were free of psychotropic medication for at least 1 month and none had previously tried either bright light therapy or dawn simulation. None had any major medical or other psychiatric conditions based on medical history, physical examinations and blood tests (including a CBC, electrolytes, TSH, T4, T3RU) and urinalysis. Subjects who smoked were excluded. Subjects who drank more than the equivalent of four cups of coffee per day were excluded. Shift workers were excluded. The institutional review board at the University of Washington approved the study. Potential subjects read and signed a consent form describing the study.

PROCEDURES.   During the 7-week study, subjects visited the clinic weekly for assessments and were asked to sleep only between the hours of 9:00 PM and 6:00 AM and keep a daily log of their sleep each week. We chose a set time for wakeup (6:00 AM) to minimize variability of the exposure to the natural sunrise among the subjects. Had we allowed subjects to sleep until 7:00 AM or 8:00 AM, some of those subjects would have been exposed to sunrise soon after awakening during February and March and, in effect, would have received "bright light" treatment soon after awakening.

The subjects were not allowed to drink alcohol or use other psychoactive drugs such as antihistamine, sleeping medication and appetite suppressants. Caffeine use was limited to the equivalent of three cups per day and no caffeine consumption in the evening. The subjects' bedrooms were required to be dark. If a streetlight or security light shined through the bedroom windows, subjects were given a sheet of black plastic to cover the windows. Subjects were asked to turn off any night lights or hall lights that might shed light into the bedroom. These hypersomnic patients typically slept throughout the night and usually did not need to get up to go to the bathroom. If this did occur, they were asked to attempt to do so only with a night light in their bathroom. During the study, they were asked to avoid any outdoor light before 8:00 AM and any direct sunlight during the day. The subjects were asked to either stay indoors if the sun were shining, or use sunglasses if they had to go outside.

If at the end of the baseline week, the SIGH-SAD remained $\geq$ 20, the subjects were randomized, stratified according to gender, into one of three treatment groups for subsequent daily use for 6 weeks:

1. Bright light therapy. The morning bright light consisted of bright (10,000 lux) light box treatment (Day Light 10,000, Day Light Technologies, Halifax, Nova Scotia) from 6:00 AM to 6:30 AM The light box was positioned on a stand and tilted toward the subject. The subjects were told to position themselves so that their eyes were 30 cm from the box, a point identified by the end of a string attached to the box. The subjects used the bright light while awake.

2. Dawn simulation. The dawn simulation (Pi Square, Inc., Shine, WA, USA) consisted of a white light with a gradually increasing illuminance (during sleep) from 4:30 AM to 6:00 AM peaking at 250 lux (similar to average room light level) in the bedroom while the subject is asleep. The signal is estimated by the equation $y = 259.5/(1 + 7862.5e^{(-0.1358x)})$ where y = the illuminance in lux and x = time in minutes after 4:30 AM. Like a natural dawn, the function is sigmoidal, beginning with a

gradual slope, followed by a steeper slope from 5:00 AM to 5:30 AM, and then a gradual slope.

3. Placebo condition. The placebo dawn simulation was administered like the active dawn, but consisted of a dim red light with a gradually increasing illuminance (during sleep) from 4:30 AM to 6:00 AM peaking at 0.5 lux. The placebo signal had a similar shape as the dawn simulation.

In both dawn simulation conditions a Remcraft model 1051 fixture was used with two Juno filter holder (#T570 4 3/4 inch size) 4 feet from the pillow. The fixtures were placed on the wall so that direct light from the fixtures would be striking the eyelids whether the patient was sleeping on his left or right side. In the white dawn condition, 100-watt R30 Philips flood lamps were used with a Roscolux gel filter #102 Light Tough Frost. In the placebo condition, 100-watt R30 Philips flood lamps was used with a Roscolux lux Medium Red (#27) gel filter; the illuminance was set on the dawn simulator to create a final peak illuminance of 0.5 lux. Subjects were asked to sleep until 6:00 AM at which time they were awakened by an alarm. If they awoke before 6:00 AM, they were asked to avoid looking at the lights, close their eyes and try to go back to sleep. Subjects assigned to the dawn simulation conditions were given sleep masks for their bed partners to use to prevent interference with their partner's sleep. A Tektronix Photometer confirmed the illuminances of the three light systems.

To increase the credibility of the dim red signal, each subject was given a statement with the description of the "Purpose of the Study," which described the three treatments (except the very low intensity of the red signal) and explicitly focused the subjects' attention on the wavelength of light and indicated that the dawn signals were much dimmer than the bright light box so that there would be no surprise at the dim level upon awakening with the dim red dawn. The statement explained that different wavelengths may have different transmittance through the eyelid and different effects on the retinas, and emphasized that a purpose of the study is to compare red and white dawns. The statement also explained that both bright light and dawn simulation had lowered the depression of SAD subjects in previous studies. The screening physician also reminded the subject of the purpose of the study. The difference in light intensities of the red and white signals was not be revealed until the end of the 7-week study.

Subjects were rated by experienced, board-certified psychiatrists who were blind to the treatment assigned using the SIGH-SAD at baseline and at the end of each treatment week. Subjects who traveled to sunny locations, experienced a shift in their work schedule not allowing compliance with the protocol, or had severe intercurrent illness were excluded from the analyses. Those who completed at least the first treatment week visit and who dropped out of the study for reasons related to the light system, such as poor clinical response, side effects or inconvenience of the light system, were included in the analyses. Subjects were told each time before seeing the raters that they should not reveal the type of treatment they are receiving.

Expectations of the response to the three treatments were assessed at baseline before the subjects saw any of the three light units. The subjects rated their expected response on a Clinical Global Improvement (CGI) scale (1 = worse, 2 = no change,

3 = slight improvement, 4 = much improvement, 5 = very much improvement). In addition, on the morning after the first treatment with their assigned light therapy, the subjects were telephoned and again asked about their expectations for that unit. At the end of each week, subjects rated their own responses to the treatment on the same CGI scale. The raters administered the SIGH-SAD and the Hypomania Interview Guide for Seasonal Affective Disorder (HIGH-SAD) (Williams et al 1988) at all visits.

At each visit, subjects were systematically asked about possible side effects by the blind raters: early morning awakening, headache, agitation, drowsiness, irritability, tight muscles, nervousness, anxiety, tremor, dizziness, fatigue nausea, diarrhea, dry mouth, anorexia, dyspepsia, constipation, excessive sweating, rash, asthenia, viral infection, upper respiratory infection, flulike syndrome, nasal congestion and hot flushes. Each item was rated as absent, mild, moderate or severe. The subjects were instructed to report any side effects that could have jeopardized the blindness of the raters (such as eye strain, a side effect characteristic of bright light) to a nonblind research assistant who simply tabulated these side effects.

Meteorological data for the Seattle metropolitan area was obtained from the University of Washington Department of Atmospheric Sciences and the National Oceanographic and Atmospheric Administration. The average daily values of the 7-day period before each visit were calculated. These data included percent possible sunshine (PPS, the percentage of time the sun was shining from sunrise to sunset), photoperiod, hours of sunshine per day and solar radiation.

Data Analysis

We defined "remission" as a SIGH-SAD score of ≤ 8 and "response" as a decrease of ≥ 50% from the baseline SIGH-SAD score. Because the SIGH-SAD at baseline was at least 20, all those who remitted by definition also responded. These categorical ratings of treatment response were assigned to each of the eight weekly assessment times of the study. Once patients responded or remitted, they continued to be assessed and could change categorical ratings over time.

All exploratory and formal statistical analyses were done with SPLUS (version 4.5 for Windows, MathSoft, Seattle, WA, USA) and the additional function libraries HMISC (Harrel 1996) and MASS (Venable and Ripley 1999). We modeled the profiles of the responses to treatment over time using Cox proportional hazards models with the Anderson–Gill extension for time-varying covariates. All missing observations from study dropouts were imputed using the last observation carried forward. In addition to base models that examined the treatment responses by treatment type alone, we explored the influence of meteorological, environmental factors and subject specific factors. These included: photoperiod, daily solar radiation, percent possible sunshine, weekly changes in sunshine, date of entry, age, gender and weekly ratings of depressive symptoms using the "typical" (H21) and "atypical" (H8) subscales of the baseline SIGH-SAD ratings. We designed our models with the aid of stepwise model selection algorithm stepAIC (Venable and Ripley 1999). Although the Cox model does not make parametric assumptions

Table 1. Characteristics of the Three Treatment Groups

	Bright light	Dawn	Placebo
N (M/F)	33 (4/29)	31 (4/27)	31 (4/27)
Mean age (SD)	40.8 (11.1)	38.3 (10.2)	42.4 (9.8)
Mean age of onset (SD)	25.1 (8.7)	25.5 (10.1)	25.1 (11.4)
Mean age at first treatment (SD)[a]	38.2 (10.5)	33.4 (10.0)	40.0 (10.0)
% College or higher	90.9	93.5	93.5
% White	97.0	87.1	87.1
% Employed	87.9	83.9	80.6
% Single	36.4	58.1	32.3
% Married	15.2	12.9	25.8
% Divorced	48.5	25.8	38.7
% Separated	0	3.2	3.2
% Bipolar II	12.5	3.2	3.2
% History of pharmacotherapy	48.5	35.5	29
% History of psychotherapy[b]	60.6	35.5	29
% History of psych hospitalization	3.0	6.5	6.5
% History of suicide attempt	3.2	2.1	4.1
% History of any psych treatment	63.6	45.2	51.6
Mean baseline SIGH-SAD (SD)	30.6 (6.2)	30.8 (5.9)	30.2 (6.6)
Mean baseline SIGH-SAD atypical ratio (SD)[c]	40.1 (8.5)	47.5 (8.8)	46.2 (9.1)
Date of entry[d]	1/15 (10/31, 2/17)	1/7 (11/22, 2/12)	1/22 (11/14, 2)

The median date of randomization into the study was Jan. 15 (Interquartile Range: Dec. 13–Jan. 27). The earliest entry was Oct. 31; the last on Feb. 17. The latest visit in the study was by a subject who finished the study on Mar. 30.

Kruskal–Wallace Nonparametric ANOVA of Differences among groups: [a]$p = .03$, [b]$p = .09$, [c]$p = .002$, [d]$p = .004$.

about the distribution of survival times, it is predicated on the assumption that the risk to each individual associated with the predictor variables are proportional (i.e., do not vary) across time. We assessed the model's assumption of proportionality of hazards for each predictor graphically and with a statistical test of the rescaled Shoenfeld residuals (Grambsch and Therneau 1994).

We present the estimates of our Cox models as the odds ratio (OR) of responding to treatment associated with the specified effect for each predictor variable, along with its 95% confidence interval and p value (two-tailed). The estimates of the treatment effects are presented as paired contrasts among the three treatment groups. The ORs for the other predictors (e.g., Hamilton score) are given for one unit changes in the predictor (e.g., 1 Hamilton point).

We compared group differences in patient demographic features using chi-square analyses and Kruskal–Wallace nonparametric ANOVA, and compared side effects with the Mann–Whitney test.

Results

Sample

Ninety-five subjects either completed the protocol or completed at least the week one visit, but dropped out for reasons related to the light system: lack of response, side effects or inconvenience. Five subjects randomized to the placebo condition dropped out because of lack of clinical response; one patient from this group dropped out due to a side effect. Two subjects in the bright light group dropped out due to side effects. Another subject in the

bright light group dropped out because of inconvenience of the light system. The characteristics of the three treatment groups are summarized in Table 1. The group were similar in most respects, but differed in some variables. The bright light group was less likely to have atypical symptoms compared to the other two groups. The mean time of entry into the study was in January; the placebo group entered the study later than the bright light group; the bright light group entered the study later than the dawn simulation group. Thus, the photoperiod was longer at the baseline and at visit 6 for the placebo group (mean hours at baseline, 9.1 hours; at visit 6, 11.5 hours) compared to the bright light group (mean hours at baseline, 8.9 hours; at visit 6, 11.2 hours) and the dawn simulation group (mean hours at baseline, 8.6 hours; at visit 6, 10.8 hours).

Remission with Treatment

The Cox proportional hazards model (Table 2) revealed that, without covariates, the dawn treatment group had significantly greater remissions than both the bright light

Table 2. Odds Ratios of Survival Model of Remissions (SIGH-SAD ≤8) by Treatment Group (No. Covariates)

	OR	95% CI	p
Dawn vs. placebo	1.51	1.07:2.13	0.02
Bright light vs. placebo	0.92	0.67:1.33	0.7
Dawn vs. bright light	1.64	1.16:2.33	0.005

Table 3. Cox Proportional Hazards Model of Treatment Remissions

Effect	OR	95% CI	p
Dawn vs. placebo	1.60	1.13:2.27	0.007
Bright vs. placebo	0.95	0.65:1.37	0.8
Dawn vs. bright	1.69	1.20:2.40	0.003
PPS (10%)	1.13	1.04:1.22	0.003
Daily hours of sunshine	1.17	1.06:1.28	0.001
Date of entry (weeks)	0.95	0.90:1.00	0.06
Hamilton 8	0.97	0.92:0.99	0.01

and placebo groups. The OR of 1.51 for the contrast between dawn simulation and placebo groups signifies a 51% greater chance of remission in any time interval under dawn treatment. The chances of remission were no different in the bright light group as compared to the placebo group. The dawn simulation group had a 64% greater chance of remission compared to the bright light group.

We augmented this Cox model with several predictors chosen by stepwise regression: percent possible sunshine, the mean daily hours of sunlight during the preceding 7-day period, and the date of entry and the 8-item "atypical symptom," H8 (Table 3). Taking into account the covariates, the dawn simulation group has a 60% greater chance of remission compared to the placebo group and a 69% greater chance compared to the bright light group. Each 10% increase in mean daily percent possible sunshine and each mean daily hour increase in sunshine predicted 13% and 17% greater odds of remission, respectively. There was a trend for each additional week delay of the date of
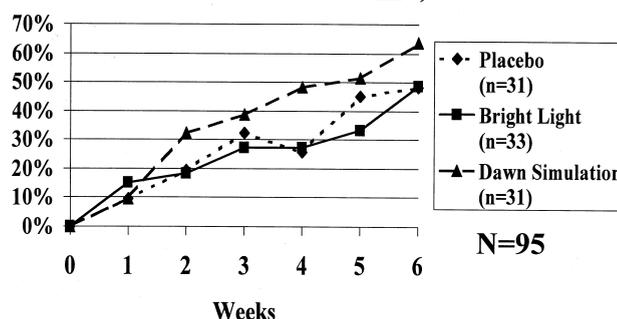

Figure 1. Percentage of remissions across weeks with dawn simulation, bright light and placebo.

entry in the fall–winter season to predict a 5% decrease in likelihood of responding. The increased severity of atypical symptoms at baseline (H8) predicted a 3% lower odds of remission.

The Cox model for remission across weeks is summarized in Table 4. The percentages of remissions across weeks are summarized in Figure 1.

Response with Treatment

The data for response (reduction of $\geq$ 50% in the SIGH-SAD) paralleled those of remission. Without covariates, the dawn simulation group had a 73% increase in the odds for response compared to the placebo group and a 78% increase in odds compared to the bright light

Table 4. Summary of Cox Model for Remission Stratified by Treatment Type

Time	No. risk	No. event	Survival	SD	Lower 95% CI	Upper 95% CI
Bright light						
Week 1	33	5	0.857	0.0594	0.7480	0.982
Week 2	33	6	0.708	0.0742	0.5767	0.870
Week 3	33	9	0.531	0.0759	0.4008	0.702
Week 4	33	9	0.403	0.0691	0.2876	0.563
Week 5	33	11	0.282	0.0580	0.1885	0.422
Week 6	33	16	0.156	0.0412	0.0928	0.261
Dawn						
Week 1	31	3	0.9077	0.0510	0.8130	1.0000
Week 2	31	10	0.6035	0.0860	0.4565	0.7979
Week 3	31	12	0.3858	0.0752	0.2632	0.5654
Week 4	31	15	0.2199	0.0549	0.1348	0.3586
Week 5	31	16	0.1146	0.0349	0.0630	0.2083
Week 6	31	21	0.0409	0.0164	0.0187	0.0897
Placebo						
Week 1	31	3	0.911	0.0490	0.8203	1.000
Week 2	31	6	0.759	0.0708	0.6322	0.911
Week 3	31	10	0.545	0.0779	0.4118	0.721
Week 4	31	8	0.415	0.0721	0.2948	0.583
Week 5	31	14	0.240	0.0566	0.1515	0.381
Week 6	31	15	0.135	0.0394	0.0765	0.239

Table 5. Odds Ratios of Survival Model of Response by Treatment Group (No Covariates)

	OR	95% CI	p
Dawn vs. placebo	1.73	1.32:2.27	0.0008
Bright light vs. placebo	0.99	0.75:1.33	0.98
Dawn vs. bright light	1.78	1.33:2.27	0.00005

Table 6. Cox Proportional Hazards Model of Treatment Responses

Effect	OR	95% CI	p
Dawn vs. placebo	1.73	1.32:2.28	0.00008
Bright vs. placebo	0.95	0.71:1.27	0.7
Dawn vs. bright	1.83	1.40:2.39	0.00001
Baseline Hamilton 21	1.05	0.96:1.08	0.006
Date of entry (weeks)	0.95	0.91:0.99	0.02
Daily hours of sunshine	1.14	1.06:1.23	0.0003

therapy group (Table 5). The bright light and placebo groups were not significantly different.

When we examined the effects of other predictors (Table 6), we again found that the weekly mean daily hours of sunshine and the date of entry influenced treatment response. We also found that the increasing severity of Hamilton ratings of "typical symptoms" (H21) at baseline predicted a greater response to treatment. Even with the covariates, the dawn group had 73% greater chance of response compared to placebo and an 83% greater chance compared to bright light. Interestingly, photoperiod did not emerge from the analyses as a significant predictor of either remission or response. The Cox model for response across weeks is summarized in Table 7. The percentages of remissions across weeks are summarized in Figure 2.

Other Measures of Improvement

The CGI at the final visit was significantly different among the three groups and was consistent with the remission and response results. Dawn simulation has a greater CGI (mean 4.34, SD 0.85) compared to either bright light (4.05, 0.96) or the placebo condition (3.57, 1.24) (ANCOVA with the baseline CGI expectation as the covariate $F = 4.0$, $p = .02$). A post hoc comparison between the bright light and placebo condition showed a nonsignificant trend for better improvement with bright light (Mann–Whitney two-tailed, $p = .12$).

Expectations

The expectations for the treatment actually received at baseline did not differ significantly among the three treatment groups (Kruskal–Wallace $\chi^2 = 0.2$, df = 2, $p = .9$). Nonremitters were no more likely than remitters to have different expectations in the dawn group (Wilcoxon ranked sum test, $p = .6$) or the placebo group ($p = .9$). In the bright light group, the remitters tended to have higher expectations than the nonremitters ($p = .08$).

Similar results were obtained for the expectations obtained on the first day of treatment. There were no significant differences among the groups (Kruskal–Wallace $\chi^2 = 3.7$, df = 2, $p = .2$). Nonremitters were no more likely than remitters to have different expectations in the dawn group (Wilcoxon ranked-sum test, $p = .7$) or the

placebo group ($p = .3$). In the bright light group, the remitters tended to have higher expectations than the nonremitters ($p = .08$).

Other Potential Confounds

Patients with a history of receiving psychotherapy had a marginally better chance of responding to treatment (OR = 1.28, 95% CI = 0.98: 1.67, $p = .07$) and a better chance of remitting (OR = 1.41, 95% CI = 0.99: 1.97, $p = .05$). A history of receiving psychoactive medication history did not influence either response or remission.

The effects of menstrual cycle on the odds of remission and response were examined in the Cox proportional hazards survival models. In both instances, menstrual cycle was rejected by the AIC based on stepwise model selection. When menstrual cycle was added manually to the model, no consistent effects were noted and the resulting statistical tests were not significant ($p > .4$).

Twenty-five percent of the sample failed to complete 4 or more weeks of sleep logs. Noncompliance with filling out the sleep logs was not significantly associated with treatment group (Fisher's test, $p = .2$) or remission ($p = .3$).

The average hours of sleep each night over each week were neither different among the three treatment groups nor associated with greater odds of remission. Among those who remitted, the dawn treatment group tended to have shorter sleep than those in the placebo group (mean difference 22 min, 95% CI = 2: 47, $p = .08$).

The effect of treatment, per se, on the time of awakening was marginal. The dawn and bright light groups awoke 15 min earlier ($p = .17$ and $p = .16$, respectively) than the placebo group, and neither differed from each other. Although the effects of remitting were negligible for both the dawn and bright light groups, the placebo group patients who remitted awoke 40 min earlier than those who did not remit ($p < .001$). Among patients who remitted, there were no intertreatment differences in wake time. Among patients who did not remit, the wake time of the placebo group was 25 min later than both the bright light ($p = .07$) and dawn groups ($p = .05$).

Table 7. Summary of Cox Model for Response Stratified by Treatment Type

Time	No. risk	No. event	Survival	SD	Lower 95% CI	Upper 95% CI
Bright light						
Week 1	33	8	0.759	0.0746	0.6259	0.9201
Week 2	33	16	0.388	0.0776	0.2620	0.5738
Week 3	33	15	0.225	0.0556	0.1388	0.3652
Week 4	33	17	0.128	0.0367	0.0733	0.2249
Week 5	33	17	0.074	0.0239	0.0393	0.1393
Week 6	33	22	0.035	0.0133	0.0166	0.0738
Dawn						
Week 1	31	8	0.71550	0.08518	0.566604	0.90353
Week 2	31	19	0.25899	0.07008	0.152390	0.44016
Week 3	31	25	0.05246	0.02359	0.021730	0.12666
Week 4	31	23	0.01732	0.00898	0.006273	0.04782
Week 5	31	25	0.00496	0.00299	0.001524	0.01616
Week 6	31	26	0.00138	0.00096	0.000355	0.00539
Placebo						
Week 1	31	6	0.7797	0.0795	0.6384	0.9523
Week 2	31	15	0.3922	0.0817	0.2607	0.5900
Week 3	31	17	0.1836	0.0518	0.1056	0.3192
Week 4	31	13	0.1130	0.0355	0.0611	0.2091
Week 5	31	18	0.0568	0.0204	0.0280	0.1150
Week 6	31	20	0.0274	0.0113	0.0122	0.0614

Side Effects

Two patients in the bright light group dropped out of the study; one subject complained of nausea and severe headache, another reported a progressive increase in difficulty going to sleep to the point that the subject was awake all night. One patient in the placebo group dropped out because of early morning awakening. The treatment groups did not differ in side effects with one exception. During the fourth treatment week, the placebo group was significantly more likely (Kruskal–Wallace chi-square = 6.67, df = 2, $p = .04$) to complain of insomnia (15.4%) compared to the bright light group (3.3%) or the dawn simulation group (0%). There were no significant differences between the dawn and bright light treatment groups in the incidences of side effects other than greater fatigue after 3 weeks (Mann–Whitney, $p < .05$) and more insomnia after 6 weeks (Mann–Whitney, $p < .05$) in the bright light group. Given the number of side effects evaluated, these differences could have occurred by chance alone. Eyestrain was reported by one subject in the bright light group and one in the dawn simulation group.

The HIGH-SAD rating scales at each visit did not differ among the three groups. Two subjects, who were unipolar, had HIGH-SAD ratings greater than 6. One subject receiving bright light therapy had a HIGH-SAD score of 10 during the first week of treatment. Another subject in the dawn group had a HIGH-SAD score of 18 during the first week of treatment. Both subjects tolerated the treatments and subsequently had HIGH-SAD scores of 6 or less.
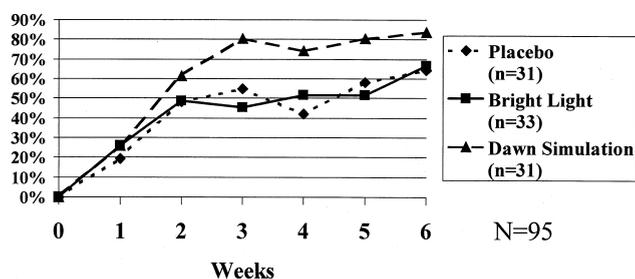
Discussion

The present study found that dawn simulation results in greater remission and response rates compared to the placebo condition, a dim red signal. Bright light therapy was similar in efficacy to the placebo. Dawn simulation in this study was superior to the bright light therapy. To appreciate some of the methodological issues that might have affected the results, it is important to consider the possible mechanisms of action of bright light therapy and dawn simulation.

Possible Mechanisms of Action of Bright Light Therapy and Dawn Simulation

Although there is no consensus about the mechanism of action of bright light therapy and dawn simulation (Lee et

Response Rates
(≥50% Decrease in SIGH-SAD)

Figure 2. Percentage of responses across weeks with dawn simulation, bright light and placebo.

al 1997), one of the major hypotheses is the phase shift hypothesis (Lewy et al 1987b, 1988). The hypothesis postulates that in the winter, under conditions of decreased morning light, the circadian rhythms become phase-delayed (shifted clockwise) relative to sleep. Thus, the phase-angle difference between sleep and other circadian rhythms, such as temperature and melatonin, is one variable of importance in the phase-shift hypothesis (Lewy and Sack 1989). Both melatonin onset and the time of the temperature minimum have been found delayed in some studies of SAD patients relative to control subjects (Avery et al 1997; Dahl et al 1993; Lewy et al 1987a; Sack et al 1990); however, other studies have found no differences (Checkley et al 1993; Eastman et al 1993; Rosenthal et al 1990; Thompson et al 1997).

Morning bright light advances (shifts counterclockwise) circadian rhythms (Lewy et al 1987b). Both Terman et al (2001) and Lewy et al (2000) have found in bright light therapy studies that phase advances of circadian rhythms are associated with clinical improvement. Although some studies have found morning and evening bright light similar in efficacy (Wirz-Justice et al 1993), many studies have found morning bright light superior to evening bright light (Avery et al 1990b, 1991; Eastman et al 1998; Lewy et al 1987a; Sack et al 1990; Terman et al 1998), and no study has found evening bright light superior to morning bright light. The superiority of morning bright light is consistent with the phase shift hypothesis because morning light phase-advances circadian rhythms.

Because bright light therapy seems to work through the eyes (Wehr et al 1987), how can the efficacy of dawn simulation be explained in subjects whose eyes are closed? The eyelids are translucent to light transmitting about 10% in the red end of the visible spectrum (>700 nm) and declining to 1–2% in green and blue end (<600 nm) (Moseley 1988). Because dim light boxes using intensities of 100–400 lux in awake subjects have been found relatively ineffective (Terman et al 1989b), how can one explain the efficacy of a dawn signal with a maximum intensity of 250 lux, which is partially blocked by the eyelids? In humans, retinal sensitivity is particularly great during the early morning hours (Bassi and Powers 1986; O'Keefe and Baker 1987). In addition, it is possible that some dawn simulation and placebo subjects opened their eyes before 6:00 AM and received a greater amount of light.

Light earlier in the morning falls on a more sensitive part of the light phase response curve (Czeisler et al 1989; Minors et al 1991). Therefore, the dawn signal may be able be able to phase advance circadian rhythms even though it is a low illuminance signal. One possible mechanism of action of dawn simulation is that it is able to phase advance circadian rhythms without awakening

the subject. In this way, dawn simulation may improve the phase angle difference between sleep and other circadian rhythms. In humans, even low levels of light (180 lux) are able to shift circadian rhythms (Boivin and Czeisler 1998). In hamsters, simulated dawn–dusk signals, compared with square pulses, are able to shift the rhythms more effectively, decrease the phase differences between the temperature and activity rhythms (Tang et al 1999) and strengthen entrainment (Boulos et al 1996). The dawn signal may possess signal properties that are not present in the square wave bright light treatment and that may be coded for by central nervous systems that respond to light. In a human study, 9 days of dawn simulation prevented the circadian phase delay observed in dim light conditions in healthy subjects (Danilenko et al 2000b). Recently, in humans, a dawn signal significantly phase advanced circadian rhythms after one simulated dawn (Danilenko et al 2000a).

The optimal time for light administration to achieve antidepressant effects is about 2.5 hours after the midpoint of sleep (Terman et al 2001). As the midpoint of sleep was 2:30 AM for our sample, the optimal time would have been about 5:00 AM, which coincides with the time of dawn simulation administration. The bright light administration in our study occurred about 3.5 hours after the midpoint of sleep.

Methodological Issues

SAMPLE.   One of the limitations of this study is that it cannot be generalized to all SAD patients. We specifically chose hypersomnic patients. Most patients with winter depression report increased sleep (Rosenthal 1993); as many as 83% of SAD patients report increased sleep duration (Rosenthal and Wehr 1987). Hypersomnia is associated with a phase delay of circadian rhythms relative to sleep (Strogatz et al 1986). Compared to nonhypersomnic patients, hypersomnic patients are more likely to respond to morning bright light treatment than to evening bright light (Avery et al 1991). There is little theoretical reason to expect the uncommon SAD patient who experiences early evening drowsiness and early morning awakening (and presumably is phase-advanced) to respond to morning bright light therapy or dawn simulation so these subjects were not included.

Although there were no manic episodes triggered by the light treatment in this study, the sample had no subjects with a history of mania and only six subjects with a history of hypomania. Caution should be exercised in treating bipolar patients with light therapies (Leibenluft et al 1995).

The random assignment of the subjects may have resulted in treatment groups that differed in factors that

might influence the probability of responding to light therapy. For example, the bright light group had a lower atypical balance score compared to the other two groups. A low atypical balance score may be a poor prognostic sign for response to bright light therapy (Terman et al 1996). Using these factors as covariates, however, bright light therapy remains inferior to dawn and no better than placebo. Although the present study is one of the largest studies of light therapies for SAD, the sample size is modest, especially compared to studies of antidepressant medication.

ENVIRONMENTAL LIGHT. More sunshine during the previous week was associated with lower depression ratings in this sample; however, when the amount of sunshine was statistically controlled, dawn's efficacy remained. Although SAD patients have reported retrospectively that they feel better during sunny weeks, only one other study has confirmed these reports with meteorological data (Molin et al 1996). Although we asked subjects to wear sunglasses during the day, we had no way of assuring compliance and did not assess their actual light exposure with ambulatory lux meters. Because of publicity about SAD, subjects may have had increased awareness of the importance of environmental light. Even exposure to bright light during the day (up to 1400 lux) may significantly phase advance circadian rhythms (Jewett et al 1997). In addition, bright light has been hypothesized to have a direct energizing effect (Lewy and Sack 1989). Much of the literature concerning SAD has emphasized the importance of photoperiod (Young et al 1997); however, photoperiod did not emerge as a factor influencing depression ratings. The photoperiod range in this study may not have been great enough to show a photoperiod effect.

STANDARDIZED REGULAR SLEEP–WAKE CYCLE. The sleep–wake schedule imposed by the study may have restricted sleep for some subjects. Because sleep deprivation can have antidepressant effects (Wirz-Justice and Van den Hoofdakker 1999), the possibility that the therapeutic effects of dawn simulation could be explained by sleep deprivation should be considered; however, according to the sleep logs, the number of hours of sleep and the time of awakening did not differ among the groups and cannot explain the results, consistent with two previous studies (Avery et al 1993, 1994).

BRIGHT LIGHT THERAPY. One of the puzzling results of the study was finding no difference between bright light and the placebo condition, the dim red signal. Some studies have found no difference between bright light and a placebo condition (Eastman et al 1992), but most controlled studies have found bright light effective (Eastman et al 1998; Lam and Levitt 1999; Terman et al 1989b; Wesson and Levitt 1998). The 10,000 lux for 30 min in the morning has been found effective in a large placebo-controlled study (Terman et al 1998). One possibility is that the bright light therapy in this study was less effective than in other studies. Comparing remission rates across studies is not optimal, but the comparison may be instructive. Although the remission rate in the present study after 6 weeks with bright light was 48%, after 4 weeks the remission rate was only 28%. This 28% rate is less than the 4-week remission rates seen in two studies using similar remission criteria, 47% (Terman et al 1998) (using a 29-item SIGH-SAD) and 58% (Eastman et al 1998) (using a 24-item SIGH-SAD). Except for one study (Terman et al 1998), most bright light studies have used a longer duration of exposure than the 30 min in this study.

The group receiving bright light may have been less likely to respond compared to the other treatment groups; they had a lower baseline atypical ratio, a factor associated with nonresponse to bright light (Terman et al 1996). However, statistically taking this factor into account, the bright light remains similar in effect to the placebo and inferior to the dawn simulation. SAD patients are not exempt from developing a depression unrelated to light deprivation. In any study of depression, life stresses, such as job and relationship problems, may confound the results.

Most previous studies of bright light showing efficacy have used a self-selected wake time rather than the 6:00 AM time imposed by this study. Forcing some of these subjects to wake up before their usual time may have been more difficult for those randomized to bright light than for those receiving dawn simulation.

The dim red signal may not have been the optimal placebo condition to use with the bright light box. Although the raters in this study were blind to the condition, two of the raters had been involved in previous dawn simulation studies, and may have had an unconscious bias toward dawn simulation that was picked up by the subjects. The dim red signal may have been a better control for the dawn simulation than it was for the bright light therapy.

Side effects from bright light may have occurred because this was a fixed-dose study. One patient dropped out because of headache and nausea from the bright light might have been able to benefit from a lower intensity of light. The subject who experienced a phase delay of her sleep probably received the bright light during the phase delay portion of her phase response curve. In a clinical setting using a more flexible dose and timing, these side effects may have been minimized or eliminated. Another subject dropped out because of the inconvenience of the bright light.

In view of the previous studies showing efficacy of bright light therapy, the lack of efficacy of bright light therapy relative to placebo in the present study may have resulted from short duration of exposure, side effects, initial group differences or other confounds not easily quantifiable such as life stresses or a better-than-expected placebo response.

PLACEBO CONDITION.   Although the remission rate in the present study after 6 weeks with the dim red signal was 48%, after 4 weeks the remission rate was only 26% which is a rate that is in between the 4-week placebo remission rates seen in two studies using similar remission criteria, the Terman study (Terman et al 1998), 5%, and the Eastman study (Eastman et al 1998), 36%.

The placebo group entered the study significantly later in the winter than the other two groups and therefore had more exposure to an expanding photoperiod. Expectations with the placebo condition were similar to the bright light and dawn simulation. Other factors besides expectations are part of the placebo response. The environmental light and standardized sleep schedule as well as the restriction of caffeine and alcohol, may have contributed significantly to the clinical response.

The regular sleep–wake cycle also created a regular light–dark cycle. All groups, including the 0.5-lux placebo signal, received a morning light treatment followed by the light in their homes that may be from 100–500 lux. Even light levels as low as 180 lux may shift circadian rhythms (Boivin and Czeisler 1998). In addition, all subjects were instructed to have a very dark bedroom at night. The very regular light–dark cycle may have been therapeutic for some subjects and may have contributed to the placebo response. Within the placebo group, the remitters awakened earlier than the nonremitters. Thus, the placebo remitters may have been exposed more consistently to earlier ambient room light and/or may have experienced a partial sleep deprivation effect compared to the placebo nonremitters.

The final illuminance of red dawn was 0.5 lux, which is slightly brighter than moonlight (about 0.2 lux). The eyelids are translucent, especially to red light (Moseley 1988). Therefore, the amount of red light received by the retinas may have been similar to a white signal of a higher illuminance. Although some have suggested that scotopic (rod-based) transduction may be responsible for shifting circadian rhythms, photopic (cone-based) transduction may also occur (Zeitzer et al 1997). Some subjects may be more sensitive to light than others (Terman and Terman 1999). Theoretically, some subjects could have responded to this "low dose" signal independent of placebo effects.

Thus, the exposure to the expanding photoperiod, the regular light–dark cycle imposed by the study, and the

theoretical benefit of the red light may explain why the placebo response in the present study is much greater than the 5% rate seen in the Terman study using the low dose negative ion generator.

DAWN SIMULATION.   The response rate of 84% and the remission rate of 61% seen in the dawn simulation group in this study are similar to those in previous studies of bright light therapy in SAD.

One of the surprising results of this study was the superiority of the dawn simulation over bright light therapy. It is possible that the dawn simulator worked better than the bright light therapy because the former helped patients better adhere to having to wake up at 6:00 AM and maintain a regular sleep–wake cycle. Although the two previous studies comparing dawn simulation and bright light therapy had methodological problems as noted previously and had short durations, these studies found bright light superior to dawn simulation (Avery et al 1992, Lingjaerde et al 1998.)

In addition, in a retrospective analysis, we compared the results of our previous studies of dawn simulation (1.5–2.0 hours dawn to 250 lux) (Avery et al 1993, 1994) and morning bright light therapy (2500 lux for 2 hours) (Avery et al 1990b, 1991). In all these studies, we used the same SAD entry criteria and the same depression rating (H21); we assessed only hypersomnic SAD subjects. Morning bright light subjects tended to have higher remission rates (greater than 50% reduction in H21 and H21 $\leq$ 8) than those receiving dawn simulation, 16/20 (80%) versus 14/23 (61%) (Fisher's Exact Test $p = .20$). Morning bright light subjects also tended to have higher response ($\geq$50% reduction in the H21) rates than those receiving dawn simulation, 18/20 (90%) versus 16/23 (70%) (Fisher's Exact Test $p = .1$). The studies were not entirely comparable. The dawn simulation trials used a parallel design; the bright light therapy studies, a crossover design. In the crossover design, some subjects receiving morning bright light started with low H21 scores; however, in this retrospective analysis bright light therapy was clearly not inferior to dawn simulation.

In the context of this retrospective analysis, the previous comparisons of dawn simulation and bright light therapy and the many studies showing bright light therapy superior to a placebo condition, one should be cautious in interpreting this finding of superiority of dawn simulation over bright light therapy. A more conservative interpretation is that dawn simulation is probably as effective as bright light therapy in the treatment of SAD.

The primary finding of this study is the superiority of dawn simulation compared to the placebo condition. This result is consistent with shorter studies with smaller samples that found dawn simulation superior to dimmer

signals. The greater efficacy of dawn simulation in this study was evident even when other factors that may influence response such as percent possible sunshine, the mean daily hours of sunshine, and baseline depression scores were statistically controlled for. The effectiveness of dawn could not be explained by differences in expectations, sleep patterns or the phase of menstrual cycle. Although there are now three studies that have found dawn simulation effective in the treatment of winter depression, replication of this finding would be important. Special attention should be given in those studies to sample selection, ambient light conditions, sleep changes and circadian rhythm shifts. Replication of the superiority of dawn simulation over placebo would mean the establishment of a convenient inexpensive treatment available for patients with seasonal affective disorder.

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