Effects of Bright Light on Sleepiness, Melatonin, and 25-Hydroxyvitamin D_3 in Winter Seasonal Affective Disorder

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Sixteen patients with winter seasonal affective disorder and 13 healthy controls were exposed to 3300 lx of cool-white fluorescent light for either 1 hour or 15 min in the morning for 2 weeks during the winter. Subjective sleepiness, melatonin concentration in saliva, and serum 25-hydroxyvitamin D_3 concentration were measured before and after the 2-week trial as well as the following summer when the patients were well. There were no significant differences in the baseline values between the patients and healthy subjects. No significant differences in the outcome measures were observed in the patients or the controls in the two groups of each after the trial. The exposure to bright light resulted in a significant decrease in subjective sleepiness early in the evening in the patients but not in the control subjects. The reduction of depressive symptoms was associated with the decrease in subjective sleepiness but not with the changes in the melatonin or vitamin D concentrations.

Key Words: Seasonal affective disorder, phototherapy, melatonin, vitamin D

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Introduction

Winter seasonal affective disorder (SAD) is characterized by classical as well as atypical symptoms of depression such as hypersomnia, leaden fatigue, increase in appetite, and carbohydrate craving especially during the evening. The onset and remission of a depressive episode occur regularly within the same period of the year. The shortening of natural photoperiod has been hypothesized to induce the emergence of symptoms during the autumn (Rosenthal et al 1984).

Treatment with bright artificial light has been shown to be effective and therefore recommended as a time-limited, first-line trial in outpatients with winter SAD (American Psychiatric Association 1993). The mechanisms of action that mediate the therapeutic response are poorly understood due to inconsistent results obtained in different experimental designs. It has been hypothesized earlier that the light-induced decrease in the ratings of subjective sleepiness primarily contributes to a specific therapeutic response (Partonen 1994). To further test this possibility, we measured subjective sleepiness at hourly intervals in the evening and in the morning of the following day before and after the trials that we carried out.

Exposure to light of 1000 lx for 1 hour is sufficient to

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suppress nocturnal melatonin to near daytime levels in healthy volunteers (McIntyre et al 1989). Even a single exposure to light of 1500 lx for 15 min early in the evening is capable of suppressing melatonin concentrations (Petterborg et al 1991). Altogether, rather high intensities but relatively short pulses of light are required to suppress melatonin synthesis in the human pineal gland. In patients with winter SAD, there is evidence that the suppression of melatonin secretion would not be critical for the antidepressant effect of light treatment (Wehr et al 1986). On the other hand, patients with winter SAD were found to be supersensitive to light in the winter and probably subsensitive to light in the summer, suggesting abnormal suppression of melatonin secretion (Thompson et al 1990). To test the possibility that the antidepressant effect of light is associated with changes in the secretion of melatonin in patients with winter SAD, we measured melatonin concentration in saliva at hourly intervals in the evening and in the morning of the following day before and after the trials that we carried out.

The antidepressant effect of bright light treatment is thought to be mediated by the processes in the eye. This hypothesis has rarely been questioned (Wehr et al 1987). In theory, the effects of artificial visible light on neurobiological processes can be mediated, in addition to the eye, through the skin (Stumpf and Privette 1989). There are absorbers of the near ultraviolet and visible radiation in the skin cell layers, and the light-induced formation of vitamin D in the skin may serve as a one of the first messenger molecules for these responses. To test whether patients with winter SAD are supersensitive to light in terms of the inducibility of vitamin D synthesis, we measured serum 25-hydroxyvitamin D_3 concentration before and within 3 days after the trials that we carried out.

All the measurements described above were also carried out in the summer, except that no experimental trial with exposure to artificial light was performed.

Methods

Subjects attending a mood and sleep disorders outpatient service were interviewed with the structured clinical instrument for the DSM-III-R diagnosis in October 1992 (Spitzer et al 1990). In addition, they were screened for the diagnosis of a major depressive episode with seasonal (winter) pattern (American Psychiatric Association 1987). For each patient, the diagnosis was assessed according to a consensus decision of two independent raters. If no consensus was achieved, the patient was excluded from the study.

Sixteen outpatients with winter SAD and 13 healthy controls participated in the study. All subjects were women. The patients with winter SAD were aged 23–55 years [mean = 40.2, standard error of the mean (SEM) = 2.2] and the healthy controls 24–64 years (mean = 41.6, SEM = 3.6). All the subjects had been free of any regular psychotropic medication for at least 1 year before the beginning of the study.

In the patients, symptoms of depression were rated with the Structured Interview Guide for the Hamilton Depression Rating Scale (HDRS)—Seasonal Affective Disorders Version (Self-Rating Format) (SIGH-SAD-SR) scale in October 1992, during the week before light treatment, on the following day after the cessation of treatment, and during the first 2 weeks of June 1993 (Williams et al 1991). This 1-week retrospective scale includes the self-rating version of the 21-item Hamilton Rating Scale for Depression and the eight-item addendum for rating atypical symptoms of depression. The correlation between the HDRS and atypical subscale scores is low, suggesting that the two subscales measure independent events. On the average, the eight atypical items contribute nearly as much as the 21-item HDRS subscale to the total score of the scale.

Healthy volunteers were referred to the study by physicians familiar with our program. Subjects were interviewed by the first author in October 1992. Their mood was rated with the SIGH-SAD-SR scale with a modification allowing the comparison of mood with the state of "as usual" instead of "when not depressed." They did not meet criteria for subsyndromal SAD nor any other mental disorder. The control subjects were considered healthy on the basis of routine clinical examinations performed by local general practioners.

Subjective sleepiness was measured with the Stanford Sleepiness Scale (SSS) anchored with "feeling active and vital, alert, wide awake" (one) and "almost in reverie, sleep onset soon, lost struggle to remain awake" (seven), indicating levels of sleepiness sensitively and reliably (Hoddes et al 1973). The scale values were presented as reversed in this study. Subjective sleepiness was rated at 20:00, 21:00, 22:00, 23:00, and 24:00 hours in the evening and at 06:00, 07:00, and 08:00 hours on the following morning. Pretreatment measurements were made during the day before the use of the lights was started. The measurements were repeated after the cessation of treatment. The collection of these data began in the evening of the cessation day. All the subjects made the measurements at their home.

Melatonin concentration in saliva was measured at 20:00, 21:00, 22:00, 23:00, and 24:00 hours in the evening and at 06:00, 07:00, and 08:00 hours on the following morning. Pretreatment measurements were made during the day before the use of the lights was started. The measurements were repeated after the cessation of treatment. The collection of these data began in the evening of

the cessation day. Samples of saliva were collected in a dark room (<3.0 lx), thereafter immediately frozen and stored at −20°C until assayed for melatonin by a radioimmunoassay with iodinated melatonin tracer and a melatonin-specific antiserum (Vakkuri 1985). The lowest detectable concentration for the method was 1.3 pg/mL (5.7 pmol/L). The intraassay and interassay coefficients of variation were from 6.7 to 9.5% and from 9.8 to 12.5%, respectively.

Pretreatment measurement for serum 25-hydroxyvitamin D_3 concentration was made during the day before the use of the lights was started. The measurement was repeated within 3 days after the cessation of treatment. Blood samples were centrifuged immediately and stored at −20°C until assayed for 25-hydroxyvitamin D_3 by competitive protein binding assay with rat serum as the source of protein (Törnquist and Lamberg-Allardt 1987). The coefficient of variation was 15% between the assays and 14% within the assays.

Experimental Procedure

The subjects were assigned to one or the other lighting condition for a parallel randomized comparison (Feinstein 1985). Seven outpatients and five healthy controls received bright light for 1 hour daily. Nine outpatients and eight healthy controls received bright light for 15 min daily.

The experimental protocols were carried out in Helsinki, Finland and its surroundings (60° N) during the decreasing photoperiod between November 7th and December 17th in 1992. Bright light was administered for either 1 hour or 15 min daily between 06:00 and 08:00 hours in the morning for 14 consecutive days.

Portable light fixtures with six 18-W cool-white (4000 K, DIN 5035) fluorescent lamps (Osram, Ltd.) were used for bright light treatment. After the lamps had warmed up, the illumination was approximately 3300 lx at the eye level measured by a silicon-photon-cell illuminance meter (Minolta Camera Co., Ltd.) from a distance of 1 m in the front of the devices.

All subjects were instructed to sit in front of and within 1 m from the light fixture. Subjects were instructed to face the lights but not to look directly into them while engaged in reading or desk work. They were requested not to sleep nor wear dark goggles. Subjects were advised to avoid bright illumination during the day and to keep their daily activities and diet as regular as possible during the study. No supplementation of vitamin D was allowed in the diet during the study.

Subjects signed an informed consent after the procedures were fully explained to them. At the beginning of the experiments, subjects received instructions on proper use of the lights. After the completion of the protocol, subjects were given the option of continuing with the light schedule of their choice for the rest of the season. The study was approved by the ethics committee of the National Public Health Institute.

Data Analysis

For this randomized clinical trial, the sample size needed for adequate statistical power was calculated. As interval scales were used, the estimates of the standard deviation were based on the pretreatment ratings of the two SIGH-SAD-SR subscales scored in October 1992. The expected difference between the effects of the two treatment strategies on mood was estimated for both subscale scores. Risk for statistical type I and II errors was accepted to be .10 each. According to these calculations, the number of subjects needed was six in each group for evaluation of the effects on the HDRS subscale ratings and seven in each group for the atypical subscale ratings.

At the beginning of statistical analysis, the distributions of the observed values were controlled for skewness and kurtosis. Subjects with missing data for a given variable were excluded from the analysis of that variable. Individual sleepiness ratings and melatonin concentrations at each of the time points were averaged to form new variables standing for the mean of three values measured during the early evening (20:00, 21:00, and 22:00 hours), the late evening (22:00, 23:00, and 24:00 hours), and the morning (06:00, 07:00, and 08:00 hours).

To evaluate and compare the responses of the patients and healthy controls to the two lighting conditions, the measurements obtained before and after treatment as well as the following summer were subjected to analysis of variance (ANOVA) with repeated measures. In the patients, the efficacy of the two lighting conditions was compared using analysis of covariate (ANCOVA) with the baseline scores as the covariate. Paired t test of mean was used for comparing the values before and after treatment within the groups, except the baseline values of early evening sleepiness were analyzed using Friedman's two-way ANOVA. Unpaired t test of mean was used for comparing the values between the groups, except the baseline values of early evening sleepiness were analyzed using Kruskal-Wallis one-way ANOVA.

Pearson correlation coefficients and Bonferroni probabilities with multiple comparisons were used for investigating the significance of associations between variables. Multiple general linear hypothesis models were formulated for analysis of the variance in the depression scores of patients (Wilkinson 1990). The two patient groups were combined for this analysis. Either the HDRS and atypical subscale scores or the changes in the scores were chosen

as dependent variables for the models. Moreover, the patient and control groups were pooled to investigate correlation coefficients and predictors of the levels of melatonin and 25-hydroxyvitamin D_3. The minimum tolerance for entry into models was .01, and the alpha-to-enter and alpha-to-remove was .15 for multiple stepwise (forward) regressions. The adjusted squared multiple R (ASMR) and the standard error of estimate (SEE) were calculated for characterization of the results. The .05 level was considered as indicating a significance in all statistical tests.

Results

Characteristics of Melatonin and 25-Hydroxyvitamin D_3 in All Subjects

Among all the subjects investigated, there was a significant correlation of the increase in the level of melatonin in the early evening after the trial with that in the late evening ($r = .78, p < .001$). The decrease in the level of melatonin in the early evening from the baseline to the summer was significantly correlated with that in the morning ($r = .50$, $p = .031$).

Furthermore, there was a significant correlation of the decrease in the level of melatonin in the morning with the decrease in the average level of 25-hydroxyvitamin D_3 after the trial in all subjects ($r = .63$, $p = .005$). This association was observed also in a regression model according to which the level of melatonin in the morning was best predicted by the level of 25-hydroxyvitamin D_3 after the trial (ASMR = .36, SEE = 5.84; $t = 3.23$, $p = .005$).

Comparisons between Patients and Controls

The ANOVA with repeated measures showed a significant treatment effect. The patients had a significantly greater response to treatment measured with the HDRS subscale ($F = 9.87$, df = 1, $p = .004$) and the atypical subscale ($F = 6.40$, df = 1, $p = .018$) compared with the controls. There was no significant effect of a lighting condition to which the individuals were assigned on the response. The baseline ratings of depressive symptoms were significantly higher in the patients compared with the control subjects (Table 1). The reduction of the HDRS subscale score was significantly greater in the patients exposed to bright light for 1 hour daily compared with the controls ($t = 3.99$, df = 9.7, $p = .003$). The differences in the HDRS and atypical subscale scores remained significant after the trial between the groups exposed to bright light for 15 min daily ($t = -3.81$, df = 13.4, $p = .002$ and $t = -2.39$, df = 10.2, $p = .038$, respectively).

The patients also had a significantly greater response to bright light in terms of reduced level of subjective sleepiness in the early evening after the trial compared with the controls ($F = 7.28$, df = 1, $p = .012$). Bright light treatment of 1 hour daily resulted in a significantly greater reduction of the level of subjective sleepiness in the early evening in the patients than in the controls ($t = -2.35$, df = 8.5, $p = .045$; see Table 2). After the trial, the patients assigned to the condition with the daily 1-hour exposure to bright light were still significantly more sleepy in the late evening compared with the controls ($t = 2.52$, df = 8.5, $p = .034$). There were no significant differences in the levels of melatonin (Table 3) or 25-hydroxyvitamin D_3 (Table 4).

Placebo light treatment of 15 min daily did not result in significant changes in the levels of subjective sleepiness, melatonin, or 25-hydroxyvitamin D_3 between the patients and the controls, except the concentration of melatonin in the morning was significantly lower after the trial in the patients compared with that in the controls ($t = 2.81$, df = 5.7, $p = .032$).

Comparisons within Patients before and after Treatment

A significant decrease in the HDRS subscale score was observed within both groups of patients after the trial

Table 1. The Ratings of Depressive Symptoms

	Mean (SEM) HDRS subscale score			Mean (SEM) atypical subscale score		
	Baseline	After	Summer	Baseline	After	Summer
Patients						
1 hour daily	15.6 (1.6)	5.9 (1.0)[a]	6.1 (1.7)[b]	7.4 (1.8)	1.9 (1.0)	1.4 (0.5)[c]
15 min daily	14.6 (2.1)	7.3 (1.1)[d]	6.4 (2.4)[e]	8.8 (2.2)	2.9 (0.8)[f]	4.1 (1.5)
Controls						
1 hour daily	5.2 (1.5)[g]	5.2 (1.7)	—	1.2 (0.6)[h]	1.2 (0.8)	—
15 min daily	6.0 (0.9)[i]	2.4 (0.7)[j]	—	2.5 (0.8)[k]	0.9 (0.3)	—

[a] $t = 5.58$, df = 6, $p = .001$; [b] $t = 3.35$, df = 6, $p = .016$; [c] $t = 3.09$, df = 6, $p = .021$; [d] $t = 3.01$, df = 8, $p = .017$; [e] $t = 3.26$, df = 8, $p = .012$; [f] $t = 2.71$, df = 8, $p = .026$; [j] $t = 3.51$, df = 7, $p = .01$ compared to the baseline within the groups.

[g] $t = -4.69$, df = 9.9, $p = .001$; [h] $t = -3.34$, df = 7.2, $p = .012$; [i] $t = -3.72$, df = 10.9, $p = .003$; [k] $t = -2.66$, df = 10.3, $p = .023$ compared with the baseline of the patients.

Table 2. The Ratings of Subjective Sleepiness

	Mean (SEM) SSS score								
	Early evening			Late evening			Morning		
	Baseline	After	Summer	Baseline	After	Summer	Baseline	After	Summer
Patients									
1 hour daily	5.0 (0.2)	3.6 (0.3)[a]	3.3 (0.4)[b]	5.9 (0.3)	4.9 (0.2)[c]	4.6 (0.3)	5.2 (0.3)	4.5 (0.4)	4.8 (0.4)
15 min daily	4.9 (0.3)	3.7 (0.2)[d]	4.2 (0.2)[e]	5.5 (0.2)	4.7 (0.4)	5.3 (0.3)	5.0 (0.4)	4.6 (0.5)	5.2 (0.2)
Controls									
1 hour daily	4.0 (0.4)	4.1 (0.1)	4.2 (0.2)	4.4 (0.6)	4.3 (0.2)	4.2 (0.3)	5.4 (0.5)	4.9 (0.5)[g]	4.5 (0.5)[h]
15 min daily	4.4 (0.3)	3.8 (0.4)	4.7 (0.5)	5.2 (0.3)	4.4 (0.3)[f]	5.6 (0.4)	5.1 (0.3)	4.7 (0.5)	5.3 (0.4)

[a] $t = -3.38$, df = 5, $p = .02$; [b] $t = -3.06$, df = 5, $p = .029$; [c] $t = -4.18$, df = 5, $p = .009$; [d] $t = -4.50$, df = 8, $p = .002$; [e] $t = -2.74$, df = 8, $p = .026$; [f] $t = -5.00$, df = 7, $p = .002$; [g] $t = -3.14$, df = 4, $p = .035$; [h] $t = -4.37$, df = 3, $p = .022$ compared to the baseline within the groups.

compared to the baseline (Table 1). There was no significant difference in the antidepressant response between the two groups ($F = .90$, df = 1,13, $p = .36$). Placebo light treatment with the daily exposure time of 15 min also resulted in a significant reduction of the atypical subscale score after the trial; however, there was no significant difference in the response measured with the atypical subscale between patients in the two groups ($F = .76$, df = 1,13, $p = .40$). Between the groups, there were no significant differences in the scores rated at the baseline or after the trial.

The lowered HDRS subscale score after the trial was best predicted by the increase in the level of melatonin in the late evening (ASMR = .48, SEE = 2.56; $t = 2.51$, $p = .041$). There was a greater correlation between the lowered HDRS subscale score and the decrease in the level of subjective sleepiness ($r = .28$) than between the former and the increase in the level of melatonin ($r = .50$) in the early evening. On the contrary, the lowered HDRS subscale score was better correlated with the increase ($r = .58$) and the decrease ($r = .13$) in the level of melatonin in the late evening and in the morning, respectively, than with the decreases ($r = .40$ and $r = .08$, respectively) in the level of subjective sleepiness.

No predictors of the reduced atypical subscale score were found. There were greater correlations between the reduced atypical subscale score and the decreases in the level of subjective sleepiness in the early ($r = .16$) and late ($r = .28$) evening than between the former and the increases in the level of melatonin in the early and late evening ($r = -.19$ and $r = -.01$, respectively). On the contrary, the reduced atypical subscale score was better correlated with the decrease in the level of melatonin ($r = .32$) than with the decrease in the level of subjective sleepiness ($r = .26$) in the morning.

There were no significant changes in the levels of subjective sleepiness between patients assigned to the two lighting conditions (Table 2). In both groups of patients, there was a significant decrease in the level of subjective sleepiness in the early evening after the trial. Exposure to bright light for 1 hour daily resulted in a significant decrease in subjective sleepiness also in the late evening after the trial.

There were no significant changes in the levels of melatonin (Table 3) or 25-hydroxyvitamin D_3 (Table 4) either within or between the two groups of patients. Detailed analysis of the melatonin concentrations measured hourly revealed no significant differences (data not shown). From the graphical plotting, it was observed that bright light treatment likely resulted in a small phase advance of the melatonin secretion rhythm. The levels of melatonin in the morning were decreased, and the profile

Table 3. The Melatonin Concentrations (pg/mL) in Saliva

	Mean (SEM) melatonin								
	Early evening			Late evening			Morning		
	Baseline	After	Summer	Baseline	After	Summer	Baseline	After	Summer
Patients									
1 hour daily	4.8 (1.9)	5.2 (1.3)	5.0 (1.0)	14.1 (4.5)	15.7 (5.8)	13.0 (3.4)	10.8 (4.2)	8.4 (1.2)	10.5 (1.6)
15 min daily	7.0 (2.0)	7.5 (2.6)	5.9 (1.6)	10.3 (2.0)	13.0 (3.5)	11.2 (3.3)	7.6 (2.9)	4.9 (1.1)	6.0 (1.0)
Controls									
1 hour daily	7.0 (1.4)	13.7 (6.4)	5.1 (0.6)	16.1 (5.1)	21.0 (8.5)	12.6 (3.7)	9.3 (2.2)	6.5 (1.6)	13.3 (3.9)
15 min daily	4.1 (0.9)	6.1 (2.1)	4.9 (0.8)	10.4 (2.6)	13.2 (3.6)	13.1 (3.6)	22.0 (5.4)	16.6 (4.0)	9.7 (2.0)[a]

[a] $t = 2.83$, df = 4, $p = .048$ compared to the baseline within the groups.

Table 4. The Serum 25-Hydroxyvitamin D_3 Concentrations (μg/L)

	Mean (SEM) 25-hydroxyvitamin D_3		
	Baseline	After	Summer
Patients			
1 hour daily	29.8 (4.5)	26.9 (4.7)	32.9 (6.6)
15 min daily	23.6 (3.0)	26.1 (4.6)	24.2 (2.7)
Controls			
1 hour daily	27.2 (4.4)	25.1 (1.6)	28.0 (2.4)
15 min daily	31.1 (5.2)	27.4 (2.9)	28.9 (2.6)

of these levels suggested that the melatonin secretion was approximately 40 min in advance compared to the baseline measurements. Furthermore, the levels of melatonin were increased from 21:00 hours to 24:00 hours, and the profile of these levels also suggested that the onset of melatonin secretion was advanced approximately 27 min.

Comparisons within Patients in the Winter and Summer

A significant decrease in the HDRS subscale score was observed within both groups of patients in the summer compared to the baseline (Table 1). There was no significant difference in the response between the two groups ($F = .03$, df = 1,13, $p = .87$). A similar decrease was observed in the atypical subscale score only within the group exposed to bright light for 1 hour in the winter. The decrease in the atypical subscale, but not in the HDRS subscale, score after the trial was significantly correlated with that from the baseline to the summer ($r = .84$, $p < .001$). There was no significant difference in the response measured with the atypical subscale between the two groups ($F = 2.42$, df = 1,13, $p = .14$). Between the two groups of patients, there were no significant differences in the scores rated at the baseline or in the summer.

The best predictors of the lowered HDRS subscale score in the summer were associated with the level of sleepiness and the reduction in that level in the early evening (ASMR = .48, SEE = 4.43; $t = -3.34$ and $p < .01$, $t = 2.95$ and $p < .05$, respectively). The best predictors of the lowered atypical subscale score in the summer were associated with the level of sleepiness in the early evening (ASMR = .28, SEE = 3.18; $t = -2.53$, $p < .05$).

The ANOVA showed that the patients responded significantly better to the change of the seasons compared with the controls, as measured with the level of subjective sleepiness in the early evening ($F = 5.96$, df = 2, $p = .005$). A significant decrease in the level of subjective sleepiness in the early evening was observed within both groups of patients in the summer compared to the baseline (Table 2). There was a significant correlation of the reduction of the level in the early evening sleepiness after the trial with that from the baseline to the summer ($r = .85$, $p = .01$). A similar correlation was observed for the reduction of the level of melatonin in the morning ($r = .90$, $p < .01$), although there were no significant differences in the levels of melatonin in the summer compared to the baseline (Table 3). No significant differences were observed in the levels of 25-hydroxyvitamin D_3 in the summer compared to the baseline (Table 4).

Discussion

Morning bright light produced a significant reduction in depressive symptoms rated with the HDRS subscale after the 2-week trial in winter SAD. Before the beginning of our study, the condition with a shorter time of exposure to light, 15 min daily, was chosen as a placebo control. Surprisingly, this condition cannot be considered as a plausible placebo, insofar as the two conditions tested resulted in an equal response rate after 2 weeks of treatment. One explanation for the observed improvement in mood can be that both treatments could have been active and exceeded the threshold of effect needed for the therapeutic outcome. Another explanation for these findings would be, however unlikely, that both treatment conditions were acting as a placebo.

The efficacy of the condition with the shorter time of daily exposure may be due to the northern location where our experiments were carried out. There was an extensive contrast between the intensity of light used for treatment and the natural illumination outdoors during the treatment hours in the morning at that time of the year. Therefore, even a short-term exposure to artificial light that we administered could have been effective enough at reducing depressive symptoms in our patients. Further, it has been hypothesized that a certain amount of photons exceeding an imaginary threshold is needed to be perceived by the eyes during light treatment for the antidepressant response. Our data show that this number of photons required for the effect may be less than concluded from the results of previous studies. A cumulative time of treatment as short as 3.5 hours produced a significant antidepressant response in the patients with a depressive episode in our study. Finally, we hypothesize that exposure to bright light is equally effective over a wide range of durations of exposure to light as it has earlier been shown to be over a wide range of intensities of light administered (Rosenthal et al 1993).

On the basis of our results, we cannot exclude that a placebo effect did contribute to the antidepressant response observed in the patients, partly because of the fact that placebo is a natural part of all modes of treatment. Moreover, we cannot reliably estimate the magnitude of

the placebo effect in our material. A reliable placebo-controlled experimental design has infrequently applied to studies on SAD (Eastman et al 1992). The fact that the expectation ratings of the subjects assigned to different conditions have not differed statistically in previous studies argues against the hypothesis that only a placebo will produce the antidepressant effect of bright light treatment.

Predictors of the antidepressant response diversed when the variation in the reduction of classical and atypical depressive symptoms were analyzed separately. This finding suggests that there may be different mechanisms underlying the onset of these two types of symptoms. In this respect, our finding agrees with a previous study indicating a biphasic emergence of symptoms during a depressive episode (Young et al 1991). The atypical depressive symptoms including fatigue, hypersomnia, and increased appetite appear to be associated with different pathogenetic mechanisms than the classical or secondary symptoms of depression. Administration of bright light is thought to be more effective in treatment of the forms of winter SAD with a predominance of neurovegetative symptoms. The finding that atypical symptoms present themselves on the first wave of an emerging depressive episode requires further attention. The atypical symptoms may represent a homeostatic need of the body to correct an erroneous signal transduction at the molecular level that will otherwise result in altered neurotransmission and the onset of a depressive episode.

In our study, there was a significantly greater decrease in subjective sleepiness with the 1-hour exposure to light daily both in the early evening after the 2-week trial as well as in the summer among the patients compared to the controls. In the other condition, there was not such a decrease from the pretreatment level. Our findings give evidence for the hypothesis that morning bright light when exposed for an adequately long time has an effect on the level of subjective sleepiness measured in the early evening. This effect is hypothesized to be associated with the antidepressant effect of light in patients with winter SAD.

We exposed the subjects to bright light in the morning, because it has given the best results with respect to the measures of success for mood and melatonin as well as other variables of diurnal rhythmicity (Dahl et al 1993). Further, it is the most suitable treatment alternative theoretically, inasmuch as we agreed with the hypothesis that a phase delay of circadian rhythms relative to the sleep–wake cycle forms the basis of the underlying pathogenetic mechanisms involved in patients with winter SAD. Interestingly, improvement of depression is closely associated with this pacing of the rhythm of melatonin, especially in cases with low pretreatment ratings of depressive symptoms (Lewy et al 1987). Exposure to light in the morning cuts off the delayed portion of nocturnal melatonin pulse and advances the phase of the circadian rhythm of melatonin secretion. Our results give little support for the phase-shift hypothesis, since an advance in the timing of the onset as well as the offset of melatonin secretion was observed after the trial; however, we did not assess the phase of the circadian rhythm of melatonin secretion, and therefore, the results in this respect should be considered with caution.

In our study, the concentrations of 25-hydroxyvitamin D_3 were found to be normal, that is from 10 to 50 μg/L, in patients with winter SAD across the seasons. Exposure to bright cool-white light during the decreasing photoperiod was not able to induce synthesis of vitamin D in the facial skin in the patients nor in the controls. Therefore, it is unlikely that the antidepressant effect of light is associated with the induction of vitamin D formation in the skin or that the state of mood can be affected by the procedures that favor the synthesis of vitamin D. Furthermore, supplementation of vitamin D has not been shown to affect mood in healthy volunteers in a study carried out previously (Harris and Dawson-Hughes 1993).

Our finding therefore disagrees with the hypothesis that a skin-derived transduction pathway of the biological effect of light on behavioral processes would exist in patients with winter SAD. However, as we did not measure the levels of 1,25-dihydroxyvitamin D_3 in this study, no conclusions can be deduced about the possible light-induced actions of this hormone in the subjects studied. Finally, our results did not give evidence for the hypothesized complementary actions between the endocrine systems of the pineal gland and the skin, although the analysis of associations discovered some intercorrelations between the levels of melatonin and those of vitamin D.

In conclusion, the effect of morning bright light treatment on subjective sleepiness in the early evening was found to be associated with the antidepressant effect of light. The light treatment protocols produced no significant effect on the melatonin secretion or the formation of vitamin D.

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