

# Effect of Light on Agitation in Institutionalized Patients With Severe Alzheimer Disease

*Sonia Ancoli-Israel, Ph.D., Jennifer L. Martin, Ph.D.  
Philip Gebrman, M.A., Tamar Shochat, D.Sc.  
Jody Corey-Bloom, M.D., Matthew Marler, Ph.D.  
Sarah Nolan, Leah Levi, M.D.*

---

**Objective:** Preliminary data suggest that morning bright light might improve symptoms of agitation, a serious problem in patients with dementia. The authors expand on an earlier pilot study by evaluating the effect of bright light therapy on agitated behavior in a large sample of patients with severe dementia. **Methods:** Ninety-two patients were randomly assigned to morning bright light, morning dim red light, or evening bright light. Agitation was rated by research staff who observed the patients every 15 minutes throughout the treatment period and by caregivers at one time-point before and one time-point after treatment. **Results:** Morning bright light delayed the acrophase of the agitation rhythm by over 1.5 hours. Bright light was associated with improved caregivers' ratings but had little effect on observational ratings of agitation. **Conclusion:** Although the result that light shifted the peak of the agitated behavior might be generalizable to patients with milder forms of AD, the fact that agitation was not ameliorated might not be. Because the suprachiasmatic nucleus (SCN) of patients with severe AD is likely to be more degenerated, and the circadian activity rhythms deteriorate as the disease progresses, it is still possible that patients with more intact SCNs, that is, patients with mild or moderate AD, might benefit from light treatment even more than those with severe AD. (*Am J Geriatr Psychiatry* 2003; 11:194-203)

---

Wandering at night, agitation, disturbed sleep, and night-day reversal are common problems for elderly adults with dementia. A patient who walks around banging into doors or who insists on leaving the house in the middle of the night presents a major problem for

the caregiver. Families often deal with these problems by having the patient institutionalized.<sup>1-3</sup> Learning more about the relationship between sleep and agitation, including "sundowning" and wandering, and examining techniques to improve agitation might post-

---

Received March 11, 2002; revised June 29, 2002; accepted July 12, 2002. From the Department of Psychiatry, University of California, San Diego (SA-I,TS,MM,SN), the Veterans Affairs San Diego Healthcare System (SA-I,TS,JC-B,MM,SN,LL), SDSU/UCSD Joint Doctoral Program in Clinical Psychology (JLM,PG), the Department of Neurosciences, University of California, San Diego (JC-B,LL), and the Department of Ophthalmology, University of California, San Diego (LL). Address correspondence to Sonia Ancoli-Israel, Ph.D.; Department of Psychiatry 116A, VASDHS, 3350 La Jolla Village Drive, San Diego, Ca 92161. e-mail: sancoliisrael@ucsd.edu

Copyright © 2003 American Association for Geriatric Psychiatry

pone, if not avoid, institutionalization for some dementia patients. This has the potential of saving billions of healthcare dollars annually,<sup>4</sup> decreasing the stress of caregivers, decreasing the amount of medication used to control agitation, and providing opportunities for elderly persons to live at home with their families for longer time periods.

Since sundowning has been linked to the light/dark cycle, some have hypothesized that sundowning and agitation may in fact be related to underlying circadian rhythm disruption.<sup>5</sup> In patients with Alzheimer disease (AD), circadian rhythms are often less robust (i.e., lower amplitude and/or less rhythmic) and may be phase-delayed (i.e., shifted later in time) when compared with cognitively intact elderly persons.<sup>6,7</sup> The strongest *zeitgeber* (time cue) that synchronizes and stabilizes circadian rhythms is bright light.<sup>8</sup>

Loss of the ability to process environmental *zeitgebers* such as night/day and dark/light has been hypothesized by Bliwise as being related to sleep disturbance in AD.<sup>9,10</sup> In our own work, we found that patients spending more time awake during the night exhibited some agitation throughout the day and night, with no consistent periods of no agitation (i.e., desynchronized agitation rhythm). Conversely, more time spent awake during the day was associated with low levels of agitation at specified times of the day and high levels of agitation at other times (i.e., more synchronized agitation rhythm).<sup>11</sup> The fragmented sleep and agitation found in nursing home patients may in fact be related to inappropriately timed sleeping and waking, perhaps secondary to a weakening of the circadian rhythms.

The amount of light most nursing home patients are exposed to is very limited. Our research has shown that nursing home patients were exposed to well under 20 minutes (median of 10.5 minutes) of bright light over 1,000 lux, and few were exposed to any light above 2,000 lux.<sup>12-14</sup> Bliwise et al.<sup>15</sup> found similar results. Yet bright light may be one of the most powerful synchronizers of circadian rhythms.<sup>8</sup> With lessened light exposure, changes in the phase (i.e., timing of internal circadian rhythms relative to clock time) seem to occur. Specifically, changes may be seen in the timing of sleep/waking, and may also occur in associated behaviors, such as agitation. Shifting the internal circadian rhythm with bright-light exposure could potentially improve the disturbed behavior.

We collected preliminary data suggesting that

morning bright light might reduce agitation in dementia patients living in nursing homes.<sup>16</sup> This study expands on the earlier pilot study by evaluating the effect of bright-light therapy on agitated behavior in a larger sample with randomized assignment to treatment conditions. We hypothesized that patients treated with morning bright light would have reduced evening agitation during the treatment period, and their agitation would be phase-advanced compared with patients exposed to comparatively dim red light, that is, the agitation rhythms of patients receiving morning bright light would peak earlier in the day during treatment than at baseline, that the strength of the rhythm would be reduced, and that these changes would not be seen in patients receiving dim red light. It was also hypothesized that patients treated with evening bright light would have their agitation phase-delayed and that this delay would also not be seen in those receiving dim red light. It was expected that agitation scores would return to near-baseline values during the posttreatment follow-up period.

---

## METHODS

### Subjects

A total of 92 patients (63 women) participated. Patients had been living in a nursing home setting for an average of 1.7 years (standard deviation [SD]: 1.9; range: 0.2–13.0 years). The mean age of patients was 82.3 years (SD: 7.6; range: 61–99 years), with no significant difference between men (80.2 years) and women (83.3 years). The average Mini-Mental State Exam (MMSE) score for the group was 5.7 (median: 4.0; SD: 5.6; range: 0–22), and the average level of education was 13.8 years (SD: 3.3; range: 5–20 years).

Before participation, the patient's legal guardian was contacted by research staff, and the study protocol was reviewed over the telephone. Once the guardian had given verbal approval for the study, a consent form, approved by the University of California San Diego Committee on the Investigation of Human Subjects, was mailed to the guardian for signature. Verbal consent was obtained from both the patient and patient's physician.

### **Scales**

Agitation was assessed both with the Cohen-Mansfield Agitation Inventory (CMAI)<sup>17</sup> and the Agitated Behavior Rating Scale (ABRS).<sup>15</sup> The CMAI is a caregiver's rating questionnaire that assesses the frequency of behavior over the previous 2 weeks. Questions relate to behaviors such as pacing and vocalizations. Aggressive behavior, physically non-aggressive behavior, and verbal agitation scores are computed, as well as a global rating of agitation, with higher scores indicating more agitation.

The ABRS<sup>18</sup> is a behavioral observation rating scale that measures the severity of five categories of agitation: manual manipulation; searching and wandering; escape behaviors; tapping and banging; and verbal agitation. The first four categories are summarized into one Physical Agitation score. All five types of agitation are scored on a scale of 0 to 3, where 0 means behavior not present; 1 means behavior present, mild intensity (e.g., patient mumbling softly); 2: behavior present, moderate intensity (e.g., patient asking question repeatedly); 3: behavior present, high intensity (e.g., patient screaming). Observers were initially trained to meet interrater agreement criteria of 90% compared with a "gold-standard" rater. The two gold-standard raters were the most experienced in administering the scale, had a theoretical understanding of agitation and dementia, and collected the majority of the observational data during the study. Interrater reliability between the gold-standard raters was maintained at above 90% and was confirmed annually. Other observers included other research staff members and advanced undergraduate student volunteers. Interrater agreement was reassessed approximately once per year. Average interrater agreement compared with the gold-standard observers was 90.7% at these reassessment periods.

To estimate level of dementia, the MMSE was administered by a trained research assistant before the study.<sup>19</sup>

### **Apparatus**

Apollo "Brite-Lite" boxes (Apollo Light Systems, Orem, UT), were used for light-treatment administration. The Brite-Lite utilizes cool-white fluorescent, non-UV, full-spectrum light bulbs with a special ballast that augments their brightness. It is shielded to limit ultraviolet and radio-frequency radiations. The box was

placed one meter from the patient, for a resulting exposure of 2,500 lux. Light was measured with a photometer at the level of the eyes to ensure the correct light exposure. Dim red light was administered with a red light box which, at 1 meter, resulted in <300 lux exposure, no brighter than typical room light levels in the nursing homes.

Actillum recorders (Ambulatory Monitoring, Inc.; Ardsley, NY) were worn by the participants for the full 18-day protocol to evaluate sleep/wake activity. Results of the sleep/wake analyses can be found in Ancoli-Israel et al.<sup>20</sup>

### **Procedures**

After consent forms had been signed, one nurse from each of three staffing shifts (day, evening, night) was asked to complete the CMAI, thus providing 24-hour information about caregiver ratings of agitation. Patients who were rated as agitated on the CMAI were classified as either being agitated in the morning (significant agitation on the day shift only;  $n=6$ ), agitated in the evening (significant agitation on the evening shift only,  $n=7$ ), or both (significant agitation both on the day and evening shifts,  $n=79$ ) and were included in the study. No patients were rated as agitated only on the night shift.

A board-certified neurologist conducted a brief neurological examination and reviewed patient medical records to confirm the diagnosis of possible or probable AD. (NINCDS-ADRDA diagnostic criteria were used.<sup>21</sup>) Patients were included if they had a diagnosis of probable or possible AD and were deemed agitated on the basis of their CMAI ratings. Patients were excluded if they had a recent or severe stroke or a primary psychiatric disorder that pre-dated the suspected onset of their dementia.

Medical charts were examined for current diagnoses and medication use as well as for the presence of cataracts and glaucoma and other preexisting eye disease. To ensure that light could enter the eye, a board-certified ophthalmologist conducted a brief ophthalmological test at the patient's bedside. Eyes were checked for cloudy optical media such as cornea, lens, or vitreous humor, which might reduce light perception. Visual acuity was tested with the Teller Acuity Card (TAC) procedure. This testing system was originally developed for use with newborns and infants. The TAC has been validated with both communicative elderly

subjects<sup>22</sup> and with non-communicative elderly nursing home patients.<sup>23</sup>

Patients were randomly assigned to one of three treatment groups: morning bright light ( $n = 30$ ), morning dim red light ( $n = 31$ ) or evening bright light ( $n = 31$ ), by block-stratified randomization, using pre-assignment by order of entry within strata. Patients were stratified by type of agitation (i.e., agitated primarily in the morning, agitated primarily in the evening, or agitated all day, on the basis of ratings from the CMAI, as described above).

Baseline agitation data were collected for 3 days, followed by 10 days of treatment (Treatment Days 1–5 and 6–10) and 5 days of posttreatment follow-up. Morning-bright and dim red light treatments were given from 0930 to 1130 hours. Evening bright light was given from 1730 to 1930, since, in this population, the patients are usually in bed and asleep by 1930 hours. Research staff sat with the patients during light treatment to ensure compliance. Patients could eat, converse, play cards, or watch television during treatment sessions as long as they remained facing the light. Research staff, using hand-held photometers, confirmed that light levels at the eye were  $>2,500$  lux each time patients changed position or activity.

The goal of the morning bright light exposure was to increase daily illumination exposure and to phase-advance both sleep and agitation. Since morning bright light is known to advance sleep phase, it was hypothesized that it may also advance agitation, thus making patients with evening agitation more likely to manifest their agitation during the daytime hours. The goal of the morning dim red light was to control for placebo effects and for effects of staff-patient interactions during treatment sessions. The goal of the evening bright light exposure was to increase daily illumination exposure and to phase-delay both sleep and agitation. Nursing staff and research staff could not be kept blind to light condition, but were told that both white and red light conditions were expected to show improvement and that the study was examining which color light would be better. Anecdotally, some nursing staff spontaneously reported that they expected the dim red light would be “soothing,” whereas bright light would be “alerting” for patients.

Agitation ratings were obtained by trained research staff observing the patient for 20 seconds every 15 minutes for 24 hours every other day for 9 days of the protocol and from 0730 to 2000 hours on the other 9 days

of the protocol. A total of 88,077 ratings were collected by 67 observers in 5 nursing homes over a 5-year period. Actillumes were worn by the subjects for the full 18-day protocol, being removed only for bathing and to download data at the end of the baseline period (3 days), at the end of the first 5 days of treatment, at the end of the second 5 days of treatment, and at the end of the posttreatment follow-up period. At the end of the 10-day treatment period and before follow-up began, nursing staff were once again asked to rate the patient on the CMAI. The same three nurses that had completed the initial ratings were asked to complete the final ratings to decrease the likelihood of interrater differences.

### Data Analysis

Data were divided into morning (wake-up to 1100 hours), afternoon (1100–1600 hours), evening (1600 hours–bedtime), and night (bedtime to wake-up). These times were chosen to divide the day symmetrically and, when possible, to include one meal per division. Outcome measures included total score on the Physical and Verbal Agitation ratings from the ABRS, and subscale scores and total scores on the CMAI. Although subjects were stratified into treatment groups based on the timing of their agitation, 81 were agitated both in the morning and evening, with only 4 agitated primarily in the evening and 5 primarily in the morning. Therefore, the effect of stratification was not examined in any of the analyses.

Parallel analyses were performed on raw data and on normal score transforms of the raw data because the distributions of the raw data across subjects were skewed. We judged statistical significance from the multivariate analyses of the normal score transforms of the physical and verbal agitation scales for ABRS analyses and the multivariate analyses of the normal score transforms of the CMAI subscales. The analyses of the two ABRS scales was a multivariate analysis of variance with treatment as a between-subject factor (morning bright light, evening bright light, dim red light) and phase of study (baseline, Treatment Days 1–5, Treatment Days 6–10, posttreatment follow-up), and time of day (morning, afternoon, evening, night) as within-subject factors. The analyses of the CMAI ratings were analysis of variance with treatment as the between-subjects factor, and phase of study and time of day (day shift, afternoon shift, night shift) as within-subject factors. The analyses

of variance were followed by preplanned contrasts (i.e., change scores): baseline versus Treatment Days 6-10 to assess treatment response and Treatment Days 6-10 versus posttreatment follow-up to assess relapse after treatment. Analyses were performed in SAS Version 8.1.<sup>24</sup>

Circadian rhythms were analyzed by fitting the five-parameter extended cosine model to the data of each subject for each phase of treatment; that is, data were modeled by a logistic transform of the standard cosine curve.<sup>11,20</sup> Briefly, the model measures the fitted function, the minimum of the fitted function; the amplitude (the difference between the minimum and the maximum of the fitted function), the acrophase (time of day of the peak of the function), and whether the function rises from its maximum more steeply or more gradually than a cosine curve.

---

## RESULTS

### Compliance With Treatment

Patients stayed in front of the light-box during treatment for an average of 105.0 minutes per 120-minute treatment session. During that time, they were asleep for 12.9 minutes, or 12.2% of the session. This resulted in an average of 92.1 minutes of treatment (median: 98.5 minutes) per 120-minute treatment session. There were no significant differences in compliance across light treatment conditions.

### Caregivers' Evaluation of Agitation: CMAI

There were no significant changes with any light treatments, in 24-hour Total Agitation ratings on the CMAI. In multivariate tests, there was a significant change in some of the subscales in agitation ratings from baseline to Treatment Days 6-10 ( $F_{[4,75]} = 3.75$ ;  $p = 0.008$ ), with nurses rating less frequent agitation after treatment across all light treatment conditions. Post-hoc analyses showed that Physical Agitation ratings significantly decreased from 10.4 to 9.6 ( $F_{[1,75]} = 7.59$ ;  $p = 0.007$ ), Verbal Agitation significantly decreased from 11.3 to 10.0 ( $F_{[1,75]} = 11.57$ ;  $p = 0.001$ ) and Total Agitation significantly decreased from 29.7 to 26.9 ( $F_{[1,75]} = 13.77$ ;  $p = 0.0004$ ).

There was also an overall effect of nursing staff shift ( $F_{[8, 340]} = 5.98$ ;  $p < 0.0001$ ), with agitation ratings being highest during the morning shift (mean: 31.2, SD: 11.0),

followed by the evening and night shifts (mean: 29.3, SD: 8.8; mean: 24.6, SD: 9.2 respectively). However, there was no overall difference among treatment groups between ( $F_{[8, 150]} = 0.19$ ;  $p = 0.993$ ) or within ( $F_{[16, 453]} = 0.99$ ;  $p = 0.46$ ) nursing shifts.

### Observed Agitation Levels: ABRS

There was no significant change with any treatment in mean 24-hour total Physical Agitation ratings nor in physical agitation levels during the morning, afternoon, evening, or night periods.

There was no significant change with any treatment in mean 24-hour total Verbal Agitation ratings. When Verbal Agitation during the four time-periods (morning, afternoon, evening, night) was examined, there was an overall decrease during the morning shift ( $p = 0.023$ ; see Table 1). However, when post-hoc simple effects were examined, statistical power was greatly reduced, and no one treatment group showed a significant improvement. There was also significant change in verbal agitation during the evening shift in the evening bright-light group ( $p = 0.011$ ; see Table 2), with increased verbal agitation during treatment. There were no other significant changes in verbal agitation in the other time periods in any of the light treatment groups.

### Agitation Rhythm

There was an overall effect of group ( $F_{[2,68]} = 3.75$ ;  $p = 0.028$ ) for Physical Agitation (Table 3). As can be seen in Figure 1, the acrophase of physical agitation for the morning bright light group ( $n = 23$ ) was delayed (i.e., was later during treatment than during baseline) by 1.63 hours ( $t_{[21]} = 2.26$ ;  $p = 0.034$ ), from 12:51 to 14:47 hours. There were no significant phase changes with morning red light ( $p = 0.83$ ) or with evening bright light ( $p = 0.34$ ). There were no significant changes in acrophase for vocal agitation. There were no significant changes in other circadian measures for any type of agitation with any treatment.

---

## DISCUSSION

Morning bright light delayed the timing of the peak of the agitation rhythm by an average of over 1½ hours, whereas evening light and dim red morning light had no effect. This does not support the original hypotheses

that morning bright light would advance the agitation rhythm, and evening bright light would delay it. In our previous study of patients with mixed dementias, morning bright light was found to delay, not advance, the sleep/wake cycle. We suggested that these elderly patients' rhythms may have been so phase-advanced as to result in morning light delaying rather than advancing the rhythms.<sup>25</sup> Our hypothesized explanation that an extreme phase-advance could explain our findings was based on the fact that light exposure of the same intensity presented at different times of the day results in different shifts in circadian rhythms. This time-dependent effect has been referred to as a phase response curve (PRC).<sup>26</sup> The PRC is, in fact, linked to the time that intrinsic melatonin secretion begins. In Figure 2, panel B, the typical PRC to light is shown schematically.

There are times of day during which light can delay (shift later) and times during which light can advance (shift earlier) circadian rhythms. In panels A and C, the PRC is shifted, resulting in effects opposite than would normally be expected.

If agitation rhythms are tied into sleep/wake rhythms, then the same shift in the PRC might also explain why morning light delayed, rather than advanced, the agitation rhythm in this group of patients. Although we hypothesized an extreme phase-advance as an explanation of these results, Harper and colleagues<sup>6</sup> studied patients with AD and found a significant phase-delay, and not a phase-advance, in both activity and temperature rhythms compared with control subjects and patients with other types of dementia. The same group of investigators also found that sundowning was related to

**TABLE 1. Effect of light treatment on mean (SD) ABRs Verbal Agitation during morning shift**

	Baseline	Treatment Days 1–5	Treatment Days 6–10	Follow-Up
Morning bright	0.19 (0.53)	0.22 (0.57)	0.22 (0.59)	0.12 (0.45)
Morning red	0.18 (0.55)	0.08 (0.36)	0.12 (0.47)	0.10 (0.40)
Evening bright	0.34 (0.71)	0.24 (0.62)	0.20 (0.56)	0.20 (0.53)
Overall	0.24 (0.61)*	0.19 (0.55)	0.18 (0.55)*	0.15 (0.47)*

Note: SD: standard deviation; ABRs: Agitated Behavior Rating Scale.

\*Baseline versus Treatment Days 6–10;  $p=0.023$ .

**TABLE 2. Effect of light treatment on mean (SD) ABRs Verbal Agitation during evening shift**

	Baseline	Treatment Days 1–5	Treatment Days 6–10	Follow-Up
Morning bright	0.23 (0.59)	0.25 (0.61)	0.27 (0.64)	0.25 (0.60)
Morning red	0.26 (0.59)	0.17 (0.52)	0.16 (0.52)	0.18 (0.53)
Evening bright	0.27 (0.63)*	0.34 (0.71)	0.33 (0.68)*	0.29 (0.67)
Overall	0.26 (0.61)	0.26 (0.64)	0.27 (0.63)	0.25 (0.61)

Note: SD: standard deviation; ABRs: Agitated Behavior Rating Scale.

\*Baseline versus Treatment Days 6–10;  $p=0.011$ .

**TABLE 3. Acrophase of Physical Agitation, as measured by the ABRs, before and after light treatment**

Treatment Group	Time Period	Mean Acrophase (time)	SD (hours)
Morning bright light ( $n=23$ )	Baseline	12:51*	4:03
	Treatment Days 1–5	14:52	2:47
	Treatment Days 6–10	14:47*	3:36
	Follow-up	13:36	4:12
Morning red light ( $n=23$ )	Baseline	16:00	2:59
	Treatment Days 1–5	15:14	3:14
	Treatment Days 6–10	15:41	3:18
	Follow-up	15:34	2:26
Evening bright light ( $n=25$ )	Baseline	14:19	4:47
	Treatment Days 1–5	13:40	3:47
	Treatment Days 6–10	14:16	3:59
	Follow-up	14:55	2:57

Note: SD: standard deviation.

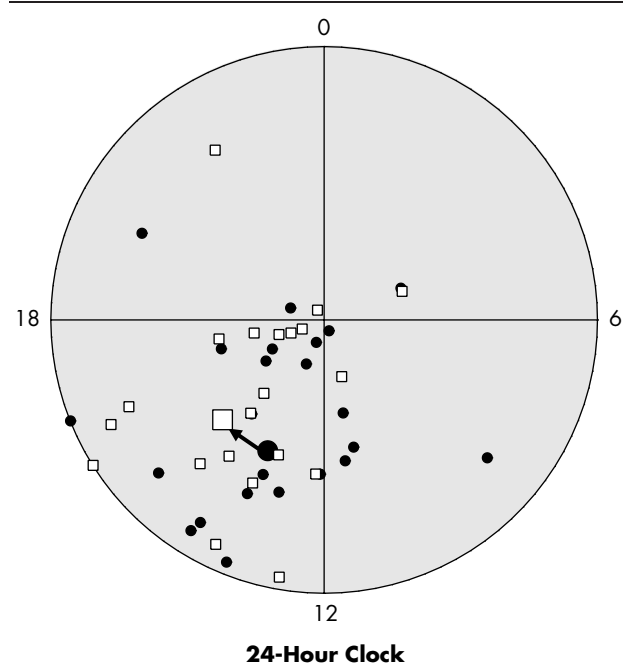
\*Baseline versus Treatment Days 6–10;  $p=0.034$ .

## Effect of Light on Agitation in AD

a phase-delay of the core body temperature.<sup>27</sup> In fact, this is not contradictory. As shown in the schemata of Figure 2, panel B, in the typical PRC, light exposure in the early part of the subjective night typically delays the circadian rhythm, whereas light exposure in the late part of the subjective night advances the rhythm. In Figure 2, panel A, the circadian rhythm is phase-advanced such that the light given from 0930 to 1130 falls in the delay portion of the cycle, whereas, in Panel C, the rhythm is phase-delayed such that the light given from 0930 to 1130 still falls in the delay portion of the cycle. It is clear however, that the pattern of response seen in these patients is not the same as that seen in cognitively intact adults.

Although one explanation of the unexpected phase shift is that it represents the response of the altered endogenous rhythm, a second explanation might be that the PRC has altered properties in patients with AD

**FIGURE 1. Acrophases of physical activity**



*Note:* Acrophase of physical activity during the morning time period was delayed in the morning-light group by 1.63 hours, from 12:51 to 14:47 ( $p < 0.034$ ). The acrophase is represented in clock hours around the circle. The radial dimension represents the rank order of the model  $F$  statistic, so that the acrophases for the better-fitting curves are plotted farthest from the center. Closed circles denote pretreatment baseline Physical Agitation acrophase, and open squares denote the Physical Agitation acrophase during Treatment Days 6-10. The large closed circle and open square represent the group baseline and treatment means, respectively (in polar coordinates).

that result in unexpected phase shifts at uncustomary circadian times. Either explanation would be theoretically possible, but only further testing and comparisons with cognitively intact age- and gender-matched control subjects will fully answer the question.

Contrary to our second hypothesis, increasing light exposure had no effect on the strength of the rhythm nor on the amplitude or mesor (mean) of the agitation rhythm. It is possible that the timing and duration of light exposure in the current study were sufficient to affect the timing of agitation but were either not long enough or not timed correctly to change the severity of the agitation. Additional studies using light at other times of the morning or evening and/or using light treatment of longer duration would be needed to answer this question.

It is important to note that the two scales used to measure behavior were likely measuring different outcome measures. As Burgio<sup>28</sup> suggested, the more standard way of assessing behavior has been rating scales that have caregivers rate the patient's behavior, usually over a time-period of a week or two. This type of scale is useful primarily when the main outcome of interest is the caregiver's evaluation of behavior. Caregiver ratings, however, must be considered in the context of the disruptiveness of agitation to caregiving itself. Also, in the nursing home setting, caregiver-to-patient ratio changes across shifts and may influence the caregivers' ratings of behavioral disturbances. Direct observation, although often neglected in gerontological research because of time and cost requirements, is a superior way of measuring behavior more accurately. Nonetheless, because agitation is problematic for caregivers, and reducing caregivers' perceptions of agitation is an important outcome in and of itself, this study examined both the caregivers' perception of the behavior and the direct observations of behavior.

The results of this study showed that increasing light exposure, whether during the morning or night, decreased caregivers' ratings of verbal agitation and physical agitation. Since ratings also improved with the dim red light, this may have been a result of an expectation effect on the part of the caregivers, particularly related to the extra attention patients received from our research staff. Observational ratings of physical agitation were unchanged in any of the light-treatment groups, although there was an overall improvement in Verbal Agitation during the morning shift. In a series of smaller studies, Okawa and colleagues<sup>29-31</sup> treated de-

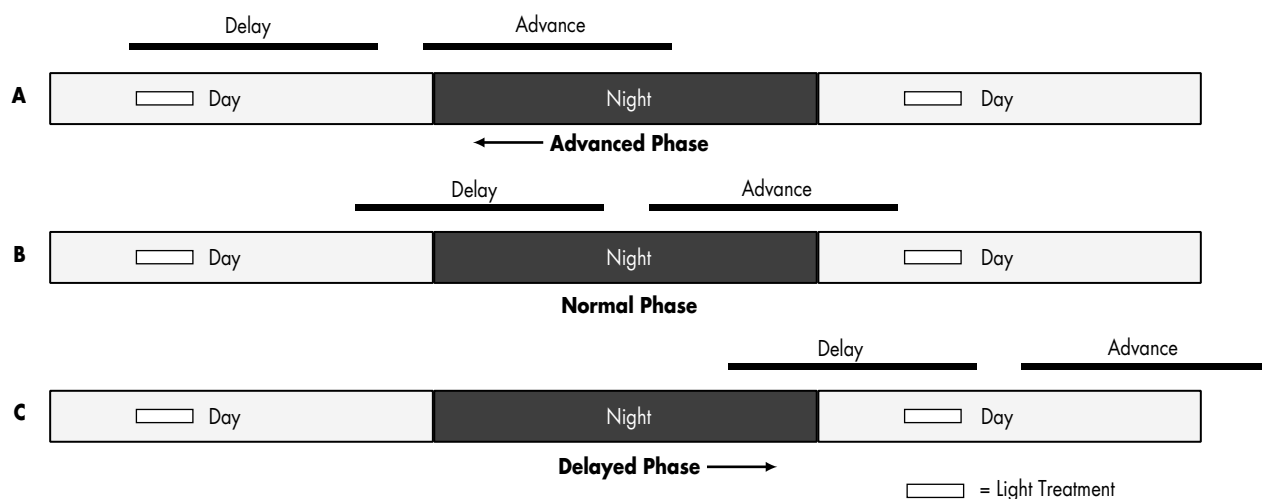
mentia patients with increased daytime activity, sleep restriction, and increased morning light exposure. Although no change was seen in the circadian temperature rhythm, clinical ratings of behavior improved with treatment. On the other hand, in two other studies of bright light, one with morning and the other with evening bright light, clinical ratings of agitation did not change.<sup>32,33</sup> Since it is the caregivers who have the difficult time with the patients, perhaps, even though objective ratings of agitation did not change, it is clinically important that caregivers perceived that agitation was reduced.

Patients with dementia and agitation are often treated with neuroleptic medication.<sup>34</sup> Yet, studies have shown that neuroleptics and antipsychotics are rarely better than placebo in reducing agitated behaviors in dementia patients.<sup>35,36</sup> Teri et al.<sup>36</sup> concluded that more effective pharmacologic, nonpharmacologic, and combination treatments are needed. This study examined a nonpharmacologic treatment of agitation, light therapy. Although overall agitation was not reduced in this study, morning bright light treatment delayed the timing of agitation. Since overall caregiver ratings of agitation decreased, it is possible that agitation now occurred at a time of day when caregivers could more easily cope with behavioral disruptions, that is, when the staff-to-patient ratio in the nursing home is higher or when

caregivers themselves are more alert. Since patients typically had lunch beginning at around 11:30 A.M., it is likely that the agitation peak levels at baseline coincided with nursing staff breaks after the patients' noontime meal. Delaying the time of the agitation peak might have decreased the burden of agitation on nursing home staff.

It is important to note that although the finding that light shifted the peak of the agitated behavior might be generalizable to patients with milder forms of AD, the fact that agitation was not ameliorated might not be. It is plausible that if patients with severe AD respond to morning light, then those with milder forms of AD will also respond. However, it does not necessarily follow that when patients with severe AD do not respond, that those in the milder stages of the disease will not respond, either. Since the suprachiasmatic nucleus (SCN) of patients with severe AD is likely to be more degenerated,<sup>37,38</sup> and the circadian activity rhythms deteriorate as the disease progresses, it is still possible that patients with more intact SCNs, that is, patients with mild or moderate AD, might respond to light treatment. Also, light may have other effects on the brain, such as an alerting effect, which may be independent of its effects on the SCN and thus its effect on entrainment of circadian rhythms, and these other effects may still affect the timing and levels of agitation. One aspect that

FIGURE 2. Phase response curves (PRC) to light stimulation, shown schematically



*Note:* Panel B represents a normal circadian rhythm. Bright light exposure during the late evening to early night (labeled "Delay") shifts circadian rhythms later. Bright light exposure during the late night to early morning (labeled "Advance") shifts circadian rhythms earlier. Panel A represents an individual who is phase-advanced. The time of light exposure that will delay the rhythm is also shifted, such that morning light treatment now delays the rhythm instead of advancing it. Panel C represents an individual who is phase-delayed. The time of light exposure that will delay the rhythm is also shifted, but morning light treatment still delays the rhythm instead of advancing it.

## Effect of Light on Agitation in AD

remains unclear, however, is whether the optimal timing of light treatment would be consistent across levels of dementia. To test these hypotheses, the current study would need to be replicated with patients in early stages of AD.

*The project could not have been completed without the cooperation of the administration, staff, and patients at the nursing homes participating in this study and without the help of Dr. Ruth Pat-Horenczyk,*

*Dr. Donald Connor, Dr. Zvezdan Nubic, Ellen Kim, and all the other UCSD staff and student volunteers who spent countless hours with the patients.*

*This work was supported by grants NIA AG08415, NCI CA85264, NHLBI HL44915, HL36005; the Department of Veterans Affairs VISN-22 Mental Illness Research, Education and Clinical Center (MIRECC), the UCSD Cancer Center, Stein Institute for Research on Aging, and the Research Service of the Veterans Affairs San Diego Healthcare System.*

### References

1. Sanford JRA: Tolerance of debility in elderly dependents by supporters at home: its significance for hospital practice. *BMJ* 1975; 3:471-473
2. Pollack CP, Perlick D, Linsner JP, et al: Sleep problems in the community elderly as predictors of death and nursing home placement. *J Community Health* 1990; 15:123-135
3. Pollack CP, Perlick D: Sleep problems and institutionalization of the elderly. *J Geriatr Psychiatry Neurol* 1991; 4:204-210
4. Walsh JK. Diagnostic and therapeutic methods in the approach to insomnia. Paper presented as part of a workshop "Clinical Practice With Outpatients of Sleep Centers," at the meeting of the World Federation of Sleep Research Societies, Cannes, France 1991
5. Bliwise DL: What is sundowning? *J Am Geriatr Soc* 1994; 42:1009-1011
6. Harper DG, Stopa EG, McKee A, et al: Differential circadian rhythm disturbances in men with Alzheimer disease and fronto-temporal degeneration. *Arch Gen Psychiatry* 2001; 58:353-360
7. Satlin A, Volicer L, Stopa E, et al: Circadian locomotor activity and core body temperature rhythms in Alzheimer's disease. *Neurobiol Aging* 2000; 16:765-771
8. Wever RA, Polasek J, Wildgruber CM: Bright light affects human circadian rhythms. *Pflugers Arch* 1983; 396:85-87
9. Bliwise DL, Yesavage JA, Tinklenberg JR: Sundowning and rate of decline in mental function in Alzheimer's disease (abstract). *Gerontologist* 1992; 32:7
10. Bliwise DL: Review: Sleep in normal aging and dementia. *Sleep* 1993; 16:40-81
11. Martin J, Marler MR, Shochat T, et al: Circadian rhythms of agitation in institutionalized Alzheimer's disease patients. *Chronobiology International* 2000; 17:405-418
12. Ancoli-Israel S, Jones DW, Hanger MA, et al: Sleep in the Nursing Home. Edited by Kuna ST, Suratt PM, Remmers JE. New York, Elsevier Press, 1991, pp 77-84
13. Ancoli-Israel S, Klauber MR, Jones DW, et al: Variations in circadian rhythms of activity, sleep, and light exposure related to dementia in nursing home patients. *Sleep* 1997; 20:18-23
14. Shochat T, Martin J, Marler M, et al: Illumination levels in nursing home patients: effects on sleep and activity rhythms. *J Sleep Res* 2000; 9:373-380
15. Bliwise DL, Carroll JS, Lee KA, et al: Sleep and "sundowning" in nursing home patients with dementia. *Psychiatry Res* 1993; 48:277-292
16. Lovell BJ, Ancoli-Israel S, Gevirtz R: The effect of bright light treatment on agitated behavior in institutionalized elderly. *Psychiatry Res* 1995; 57:7-12
17. Cohen-Mansfield J, Marx MS, Rosenthal AS: A description of agitation in a nursing home. *J Gerontol* 1989; 44:M77-M84
18. Bliwise DL, Lee KA: Development of an agitated behavior rating scale for discrete temporal observations. *Journal of Nursing Measurement* 1993; 1:115-124
19. Folstein MF, Folstein SE, McHugh PR: Mini-Mental State: a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975; 12:189-198
20. Ancoli-Israel S, Gehrman PR, Martin JL, et al: Increased light exposure consolidates sleep and strengthens circadian rhythms in severe Alzheimer's disease patients. *Behavioral Sleep Medicine* 2003; 1:22-36
21. McKhann G, Drachman D, Folstein M, et al: Clinical Diagnosis of Alzheimer's Disease: Report of the NINCDS-ADRDA Work Group Under the Auspices of the Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 1984; 34:939-944
22. Marx MS, Werner P, Fridman P, et al: Visual acuity estimates in the aged. *Clinical Vision Science* 1989; 4:179-182
23. Marx MS, Werner P, Cohen-Mansfield J, et al: Visual acuity estimates in noncommunicative elderly persons. *Investigative Ophthalmology and Visual Science* 1990; 31:593-596
24. SAS Institute Inc: SAS/STAT User's Guide, Version 8. Cary, NC, SAS Institute Inc, 1999
25. Ancoli-Israel S, Martin JL, Kripke DE, et al: Effect of light treatment on sleep and circadian rhythms in demented nursing home patients. *J Am Geriatr Soc* 2002; 50:282-289
26. Lewy AJ, Bauer VK, Ahmed S, et al: The human phase response curve (PRC) to melatonin is about 12 hours out of phase with the PRC to light. *Chronobiology International* 1998; 15:71-83
27. Volicer L, Harper D, Manning BC, et al: Sundowning and circadian rhythms in Alzheimer's disease. *Am J Psychiatry* 2001; 158:704-711
28. Burgio L: Interventions for behavioral complications of Alzheimer's Disease: behavioral approaches. *Int Psychogeriatr* 1996; 8:45-52
29. Okawa M, Hishikawa Y, Hozumi S, et al: Sleep-wake rhythm disorder and phototherapy in elderly patients with dementia, in *Biological Psychiatry*. Edited by Racagni G, Brunello N, Fukuda T. Amsterdam, The Netherlands, Elsevier North-Holland, 1991, pp 837-840
30. Okawa M, Mishima K, Hishikawa Y, et al: Circadian rhythm disorders in sleep-waking and body temperature in elderly patients with dementia and their treatment. *Sleep* 1991; 14:478-485
31. Mishima K, Okawa M, Hishikawa Y, et al: Morning bright light therapy for sleep and behavior disorders in elderly patients with dementia. *Acta Psychiatr Scand* 1994; 89:1-7

32. Walters A, Hening W, Chokroverty S, et al: Opioid responsiveness in patients with neuroleptic-induced akathisia. *Movement Disorders* 1986; 1:119-127
33. Lyketsos CG, Lindell Veiel L, Baker A, et al: A randomized, controlled trial of bright light therapy for agitated behaviors in dementia patients residing in long-term care. *Int J Geriatr Psychiatry* 1999; 14:520-525
34. Billig N, Cohen-Mansfield J, Lipson S: Pharmacological treatment of agitation in a nursing home. *J Am Geriatr Soc* 1991; 39:1002-1005
35. Schneider LS, Pollock VE, Lyness JA: A metaanalysis of controlled trials of neuroleptic treatment in dementia. *J Am Geriatr Soc* 1990; 38:553-563
36. Teri L, Logsdon RG, Peskind E, et al: Treatment of agitation in Alzheimer's disease: a randomized, placebo-controlled clinical trial. *Neurology* 2000; 55:1271-1278
37. Swaab DF, Fliers E, Partiman TS: The suprachiasmatic nucleus of the human brain in relation to sex, age, and senile dementia. *Brain Res* 1985; 342:37-44
38. Swaab DF, Roozendaal B, Ravid R: Suprachiasmatic Nucleus in Aging, Alzheimer's Disease, Transsexuality, and Prader-Willi Syndrome. Edited by de Kloet ER, Wiegant VM, de Wied D. New York, Elsevier, 1987, pp 301-310