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Effect of morning bright light treatment for rest–activity disruption in institutionalized patients with severe Alzheimer's disease

Glenna A. Dowling,[1] Erin M. Hubbard,[2] Judy Mastick,[2] Jay S. Luxenberg,[3] Robert L. Burr[4] and Eus J. W. Van Someren[5]

[1] *University of California, San Francisco, CA, U.S.A.*
[2] *Institute on Aging, Research Center, San Francisco, CA, U.S.A.*
[3] *The Jewish Home, San Francisco, CA, U.S.A.*
[4] *University of Washington, Seattle, WA, U.S.A.*
[5] *Netherlands Institute for Brain Research and VU University Medical Center, Amsterdam, The Netherlands*

ABSTRACT

Background: Disturbances in rest–activity rhythm are prominent and disabling symptoms in Alzheimer's disease (AD). Nighttime sleep is severely fragmented and daytime activity is disrupted by multiple napping episodes. In most institutional environments, light levels are very low and may not be sufficient to enable the circadian clock to entrain to the 24-hour day. The purpose of this randomized, placebo-controlled, clinical trial was to test the effectiveness of morning bright light therapy in reducing rest–activity (circadian) disruption in institutionalized patients with severe AD.

Method: Subjects ($n = 46$, mean age 84 years) meeting the NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke – the Alzheimer's Disease and Related Disorders Association) AD diagnostic criteria were recruited from two large, skilled nursing facilities in San Francisco, California. The experimental group received one hour (09:30–10:30) of bright light exposure (≥ 2500 lux in gaze direction) Monday through Friday for 10 weeks. The control group received usual indoor light (150–200 lux). Nighttime sleep efficiency, sleep time, wake time and number of awakenings and daytime wake time were assessed using actigraphy. Circadian rhythm parameters were also determined from the actigraphic data using cosinor analysis and nonparametric techniques. Repeated measures analysis of variance (ANOVA) was used to test the primary study hypotheses.

Correspondence should be addressed to: Glenna A. Dowling. University of California, San Francisco, Department of Physiological Nursing, 2 Koret Way, Room N631, San Francisco, CA 94143-0610, U.S.A. Phone +1 415 502 7791; Fax: +1 415 476 8899. Email: glenna.dowling@nursing.ucsf.edu. Received 12 Mar 2004; returned for revision 4 May 2004; revised version received 27 May 2004; accepted 27 May 2004.

Results and conclusion: Although significant improvements were found in subjects with aberrant timing of their rest–activity rhythm, morning bright light exposure did not induce an overall improvement in measures of sleep or the rest–activity in all treated as compared to control subjects. The results indicate that only subjects with the most impaired rest–activity rhythm respond significantly and positively to a brief (one hour) light intervention.

Key words: Actigraphy, sleep, dementia, circadian rhythms, light, nursing home

Introduction

Sleep disturbances are one of the primary reasons for Alzheimer's disease (AD) patients to be institutionalized (Hope *et al.*, 1998; Yaffe *et al.*, 2002). These disturbances negatively impact quality of life for both patients and caregivers. Neuroanatomical and neurochemical alterations and deterioration that underlie the AD process, genetic factors (e.g. state–trait variability, apolipoprotein E (APOE) carrier status), institutionalization, and decreases in external zeitgebers that influence circadian rhythms (e.g. bright light) probably all contribute to the etiology of the rest–activity disruptions (Bliwise *et al.*, 1995; Yesavage *et al.*, 2002; 2003; 2004). Disruptions include severely fragmented nighttime sleep (increased number and duration of awakenings), decreased total nighttime sleep time, and increased daytime sleep. Pharmacologic treatment for sleep disruption has proved to be only minimally effective and is often associated with numerous and serious side-effects (McCurry and Ancoli-Israel, 2003; Yesavage *et al.*, 2003). Administration of melatonin to treat sleep disturbances in dementia has been studied. Although results indicate that melatonin has minimal or no side-effects, its efficacy in reducing disruptions in the rest–activity rhythm in AD patients remains inconclusive, and two recent studies found it to be ineffective (Serfaty *et al.*, 2002; Singer *et al.*, 2003).

Exposure of the eyes to light of adequate intensity and duration at the appropriate time of day can have profound effects on the quality, duration and timing of sleep. The effect of light on the circadian timing system is mediated by the retinohypothalamic tract and the daily light–dark cycle is the primary synchronizer responsible for entrainment of the sleep–wake rhythm to the 24-hour day (Hoban *et al.*, 1991). In an institutional environment where light levels tend to be very low, residents may not be exposed to enough bright light to entrain to the 24-hour day (Campbell *et al.*, 1988; Shochat *et al.*, 2000). Bright light treatment has also been shown to ameliorate sleep–wake cycle disturbances in some subjects with AD (Satlin *et al.*, 1992).

The purpose of this study was to test the effect of morning bright light exposure on nighttime sleep, daytime wake time, and the rest–activity rhythm.

We hypothesized that administration of bright light treatment would improve nighttime sleep (e.g. increase sleep efficiency, decrease the number of nighttime awakenings), increase daytime wake time, and strengthen the rest–activity rhythm.

Method

The 46 participants in this study were recruited from two large, long-term care facilities in San Francisco, California. Staff from these facilities identified residents who experienced rest–activity disruption and were diagnosed with AD. Rest–activity disruptions included insomnia, frequent nighttime awakenings, wandering at night, unusually early morning awakenings, "sundowning," and excessive daytime sleepiness. Chart reviews were conducted to confirm that potential subjects met the following criteria for inclusion: a diagnosis of AD according to the National Institute of Neurological and Communicative Disorders and Stroke – the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria (McKhann *et al.*, 1984), the ability to perceive light, and a stable medication regimen. Potential subjects were excluded if they had other neurological diagnoses (e.g. Parkinson's disease) or were regularly taking valerian, melatonin or sleeping pills. No subjects were excluded on the basis of gender, race, or other medication usage. Informed consent was obtained from responsible parties as approved by the Institutional Review Board. Subjects were, on average, 84 years of age (SD = 10, range 60–98) with a mean Mini-mental State Examination (MMSE; Folstein *et al.*, 1975) score of 6.7 (SD = 6.8, range 0–23). Seventy-eight percent of subjects were female and 22% male. The ethnic breakdown of the sample was: 80.4% Caucasian, 13.0% African American, 4.4% Latino, and 2.2% Asian.

Rest–activity data were collected using the Actiwatch® activity monitor (AW-64, Mini Mitter Co. Inc., Bend, OR, U.S.A.). Actiwatches are compact, wrist-worn, battery-operated activity monitors whose physical characteristics are similar to a small wristwatch. These monitoring devices use a motion sensor known as an "accelerometer" to monitor the occurrence and degree of movement-induced accelerations. The sensor then integrates the degree and speed of motion and produces a small signal whose magnitude and duration depend on the amount of movement-induced accelerations. The signal is amplified and digitized by the on-board circuit. This information is stored in memory on board the device as activity counts in one-minute epochs. Actiwatches were placed on each subject's dominant wrist and a nylon locking cable was affixed through the watchband to deter removal by the subject. Subjects wore the Actiwatch continuously during each monitoring period.

Actigraph data have been shown to correlate well with polysomnography results in healthy elderly people (Colling *et al.*, 2000). Actigraphy provides a feasible technique for studying the rest–activity rhythm in institutionalized patients with dementia and correlates well with both electroencephalogram recordings and direct observation (Ancoli-Israel *et al.*, 1997; Singer *et al.*, 2003).

This study was conducted in two phases. Phase One was designed to compare morning bright light exposure with usual room light exposure; subjects were randomly assigned to either the bright light or usual light conditions. Phase Two was designed to compare morning with afternoon bright light exposure; subjects were randomly assigned to either the morning bright light or afternoon bright light conditions. Subjects exposed to morning bright light in both Phases One and Two did not differ statistically on any demographic characteristics. We have therefore included subjects who received morning bright light exposure in either Phase One or Phase Two in these analyses.

The study protocol was 12 weeks in duration: baseline (week 1), intervention (weeks 2–11), and postintervention (week 12). We report here on the variables assessed at baseline (week 1) and during the last week of the 10-week intervention period (week 11). Actigraphs were worn for six days and seven nights at baseline and for five days and nights during the last week of the intervention. Subjects in the experimental condition received one hour of bright light exposure (09:30–10:30, $>$ 2500 lux in gaze direction) Monday through Friday for 10 weeks. Study staff who conducted activities for the experimental group worked closely with recreational therapy departments at both locations to ensure that they were appropriate for the patients and similar to those regularly scheduled. The experimental group's activities were held in a brightly lit area, either outdoors or in an indoor space with expansive surrounding windows to let in ample amounts of natural light. APOLLO Brite Lite IV^{TM} (Orem, UT, U.S.A.) light boxes were used, when necessary, to supplement the natural ambient light to ensure that light in the gaze direction of the experimental group was at least 2500 lux. The light boxes measured $23 \times 12 \times 4$ inches and provided 10,000 lux exposure at 26 inches and 2500 lux exposure at 4 feet. Light levels were monitored each day during the intervention with a Cal LIGHT 400^{TM} (Auburn Hills, MI, U.S.A.) calibrated precision light meter. The control group received usual indoor light (150–200 lux) and participated in their regularly scheduled activities in their usual location.

Actigraphy data were analyzed using the Actiware^{TM} Sleep Version 3.2 program. For the purposes of these analyses, nighttime was defined as 20:00 to 08:00 and daytime was defined as 08:00 to 20:00 as these times corresponded to the institutional bed and rise times. Actual sleep and wake times were not recorded as there was insufficient staff to observe and record these parameters and the subjects were unable to use the event marker on the Actiwatches or

accurately record in a diary. The primary outcome variables were sleep efficiency (actual sleep time divided by the 12-hour nighttime period, and multiplied by 100), nighttime sleep time, nighttime wake time, and number of nighttime awakenings; daytime wake time was also examined.

Additional circadian outcomes were computed by two methods. Traditional parametric cosinor analyses (Ancoli-Israel *et al.*, 2002; Fontana Gasio *et al.*, 2003; Refinetti, 2000) and nonparametric techniques (Van Someren *et al.*, 1999) were used to estimate each subject's 24-hour rest–activity rhythm.

For each subject and time condition, the parametric 24-hour fixed period cosinor model was fit to the $\log_e$ transformed actigraphy data (counts per minute). Circular decimal clock time was re-represented as two trigonometric dummy variables (sine and cosine projections on 06:00 and 24:00, respectively), which were used as simultaneous independent variables in a least-squares multiple regression. The decision to $\log_e$ transform the raw count data prior to analysis was based on the highly skewed empirical distribution of the activity count data, and also was intended to ensure a larger relative weighting of the fit to the conceptually important lower activity nocturnal period. The $\log_e$ transformation makes the effective data analysis weight-of-evidence for each time point more uniform and balanced over the entire 24-hour period.

The resulting within-subject coefficient estimates were then transformed to compute standard interpretive cosinor parameters (e.g. amplitude, acrophase) as well as a goodness-of-fit index for the model (R^2). These within-subject cosinor summary parameters then became variables in the across-subject analyses.

The cosinor model is a simple, effective and robust first-order description of the average level, magnitude of swing, and general timing of a subject's diurnal activity pattern. However, the model may be too simple to capture some important qualitative aspects of the 24-hour activity patterns. In particular, the model presumes a simple cosinusoidal shape to the 24-hour pattern, with a 12-hour:12-hour cycle, and an exact 12-hour difference between the peak acrophase and the nadir. Adult human activity patterns tend to have a cycle that is more like 16-hours:8-hours, an average shape that looks more like a square wave than a pure cosinuoid, and no formal constraint on the relative timing of acrophase and nadir. Thus, in addition to considerable random components to the residual variance of the cosinor model that are related to the minute-by-minute fluctuations in measured activity counts, there may also be substantial structural model mismatch error forced into the overall error term. The fitted acrophase becomes a compromise between the timing of the true activity peak and nadir, which may not be an efficient representation of either. The activity levels that are predicted by the fitted cosinor model may significantly overestimate the true average levels measured during the typically shorter sleep/rest period.

This motivates the addition of other summary measures that are more sensitive to the characteristics of the empirical 24-hour activity profile.

Nonparametric techniques were used to assess the following circadian parameters (Van Someren *et al.*, 1999):

a) interdaily stability (IS) – quantifies the degree of resemblance between activity patterns of individual days, theoretical range of 0–1, higher values indicate a more stable rhythm;
b) intradaily variability (IV) – quantifies the fragmentation of periods of rest and activity, theoretical range near 0 for a sine wave up to 2 for Gaussian noise and even higher values when a definite ultradian component with a period of 2 hours is present, higher values indicate a more fragmented rhythm;
c) L5 – sequence of the five least active hours in the 24-hour average activity profile. Average activity during L5 provides an indication of trough or nadir of the rhythm (i.e. regularity and restfulness of sleep periods), lower values indicate more restful sleep;
d) M10 – sequence of the 10 most active hours in the 24-hour average activity profile. Average activity during M10 provides an indication of the peak of the rhythm, that is how active and regular the activity (wake) periods are;
e) relative amplitude (RA) – reflects the normalized difference between the most active 10-h period and the least active 5-hour period in an average 24-hour pattern, theoretical range from 0 to 1, higher values indicate a stronger rhythm.

Results

Compliance with actigraphy

Subjects tolerated the Actiwatches® well, with 84% never removing the device during the 12-day monitoring period (six days and seven nights at baseline and five days and nights during the last week of the intervention). On average, there were 152 hours of valid data for the baseline assessment (SD = 9, range 125–156) and 105 hours of valid data for the end of intervention assessment (SD = 7, range 69–108).

Exposure to light treatment

Exposure to at least 2500 lux during the intervention was assured by daily light meter readings, which yielded a mean of 7500 lux (SD = 9500; range 2500–65 500). Total exposure to the light treatment was recorded for each patient and reflected absence due to illness or holiday, and approximate percent of the intervention missed (eyes closed/sleeping, toileting time, etc.). The percentage of exposure to the light treatment was calculated by dividing the hours of intervention received by the total possible number of intervention hours

(50 hours over the 10-week intervention period). The mean exposure to the light treatment over the entire intervention period was 73% (SD = 17.5, range 28–98).

Nighttime sleep

Mean values for the nighttime sleep variables by group are presented in Table 1. Using an intent-to-treat analysis, where all subjects who were randomized were included in the analyses, repeated measures analysis of variance (ANOVA) revealed no significant changes in sleep efficiency, sleep time, wake time, or number of awakenings in the experimental group as compared to the control group.

Daytime wake time

Mean values for the daytime wake time by group are presented in Table 1. There was no significant difference between the experimental and control groups on daytime average wake time.

Circadian rhythms

Cosinor analyses of baseline data revealed relatively low R^2 values (see Table 1) indicating a poor goodness of fit of this model with the data. Figure 1 illustrates the distribution of the cosinor parameters during week 1 and Figure 2 for week 11. In these polar plots, the acrophase is represented on the angular axis with 0 representing midnight, 6 representing 06:00, 12 representing 12:00 noon, and 18 representing 18:00. The rhythm amplitude is depicted by the position on the radial axes. There were no significant differences in R^2, amplitude, or acrophase between the groups. There was a trend ($p < 0.09$) toward significance in amplitude with improvement in the experimental group and worsening in the control group. There was also a trend ($p < 0.08$) toward significance in the rest–activity acrophase. The average peak of the rest–activity rhythm delayed in the control group from 13:32 to 15:34 (122 minutes) and advanced slightly in the experimental group from 15:29 to 15:25 (4 minutes). There were also no significant differences in the intent-to-treat analyses between groups on variables derived from the nonparametric circadian rhythm analyses (i.e. IS, IV, L5, M10, or RA).

There was a wide variability in L5 onset times at baseline as illustrated in Figure 3, where position on the angular axis corresponds to clock time. L5 is an indication of the rest–activity nadir and defined as the five least active hours in the 24-h average curve (Van Someren *et al.*, 1999). Thus, the optimal timing of the five least active hours would be during bedtime. In this study, the usual institutional bedtime was 20:00 and rise time was 08:00. During post-hoc analysis, we therefore categorized subjects into two groups based on L5 onset time. Non-aberrant onset times were defined as those between 20:00 and

Table 1. Means and standard deviations for actigraphy measured nighttime and daytime variables, parametric cosinor and nonparametric analyses of rest–activity rhythm data; $n = 46$ (17 control, 29 experimental)

	BASELINE (WEEK 1)	END OF INTERVENTION (WEEK 11)
NIGHTTIME		
Sleep efficiency		
Control	66.88 (19.24)	71.14 (16.78)
Experimental	63.02 (19.57)	66.64 (15.85)
Sleep time (hours:minutes)		
Control	8:01 (2:18)	8:32 (2:00)
Experimental	7:33 (2:20)	7:59 (1:54)
Wake time (hours:minutes)		
Control	3:58 (2:18)	3:27 (2:00)
Experimental	4:25 (2:20)	3:59 (1:54)
Number of awakenings		
Control	34.88 (13.65)	37.99 (11.65)
Experimental	41.56 (16.03)	42.88 (16.63)
DAYTIME		
Day wake time (hours:minutes)		
Control	7:21 (2:43)	6:34 (2:50)
Experimental	6:36 (2:30)	6:24 (2:38)
COSINOR		
R^2		
Control	0.17 (0.14)	0.16 (0.13)
Experimental	0.09 (0.09)	0.11 (0.09)
Amplitude		
Control	1.32 (0.83)	1.20 (0.79)
Experimental	0.89 (0.56)	1.05 (0.70)
Acrophase (hours:minutes)		
Control	13:32 (2:37)	15:34 (3:40)
Experimental	15:29 (3:19)	15:25 (4:40)
NONPARAMETRIC		
Interdaily stability (IS)		
Control	0.47 (0.18)	0.51 (0.15)
Experimental	0.36 (0.16)	0.47 (0.18)
Intradaily variability (IV)		
Control	1.17 (0.45)	1.20 (0.34)
Experimental	1.27 (0.35)	1.33 (0.32)
L5		
Control	40.75 (49.20)	27.18 (33.79)
Experimental	61.27 (99.24)	38.72 (62.33)
M10		
Control	149.22 (103.74)	133.42 (108.16)
Experimental	182.32 (302.25)	221.20 (541.13)
Relative amplitude (RA)		
Control	0.62 (0.21)	0.68 (0.15)
Experimental	0.52 (0.22)	0.59 (0.22)

L5 = sequence of the five least active hours in the 24-hour average activity profile; M10 = sequence of the 10 most active hours in the 24-hour average activity profile.

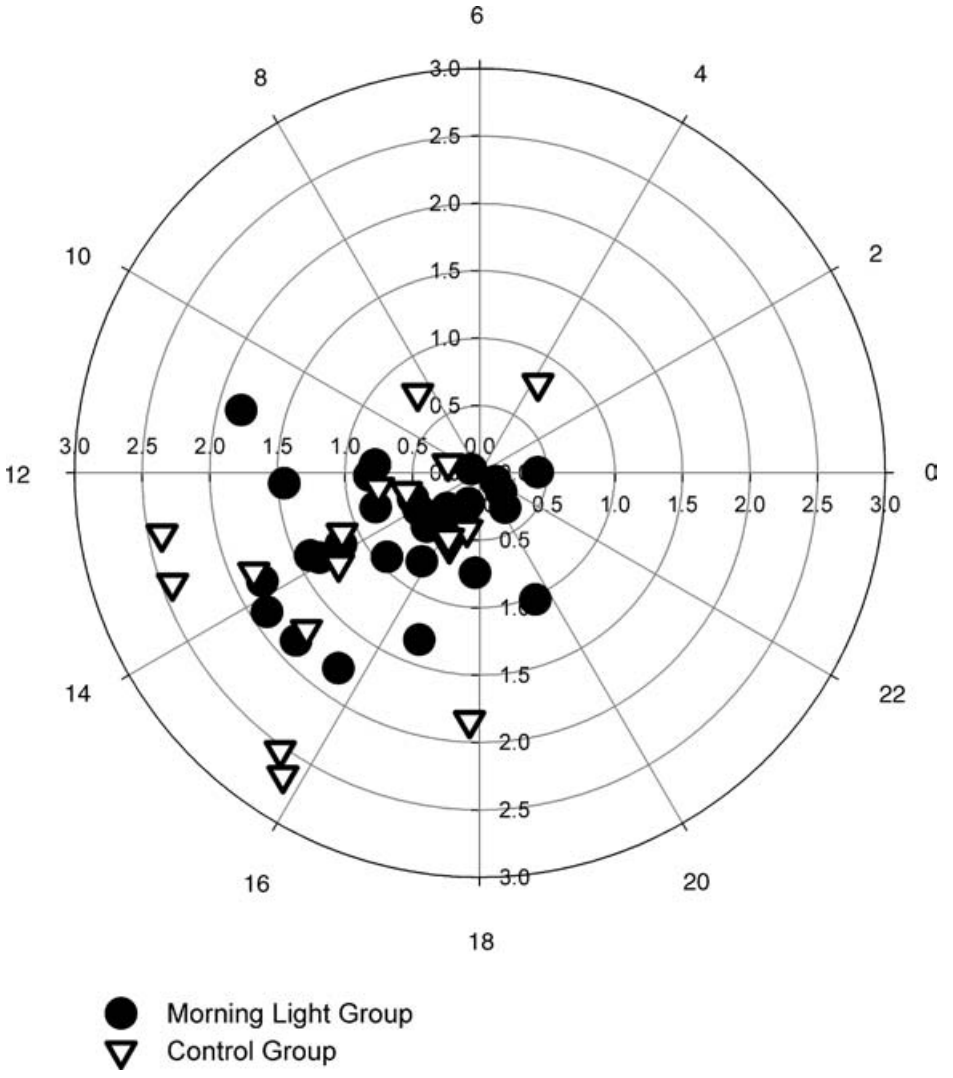

Figure 1. Cosinor-derived rest–activity acrophase (peak) and amplitude at week 1 illustrates marked between-subject variability. Position on the angular axis corresponds to clock time, position on the radial axis corresponds to amplitude.

03:00 and aberrant times as between 03:01 and 19:59. Using this definition, 13 subjects were aberrant ($n = 11$ experimental, $n = 2$ control) and 33 subjects were non-aberrant ($n = 18$ experimental, $n = 15$ control). Paired t-tests on data from subjects in the experimental group with aberrant L5 onset times at baseline demonstrated a significant improvement in IS ($p < 0.02$) and a trend toward increased RA ($p < 0.08$) at the end of intervention compared to baseline. Paired t-tests on data from subjects in the experimental group with non-aberrant L5

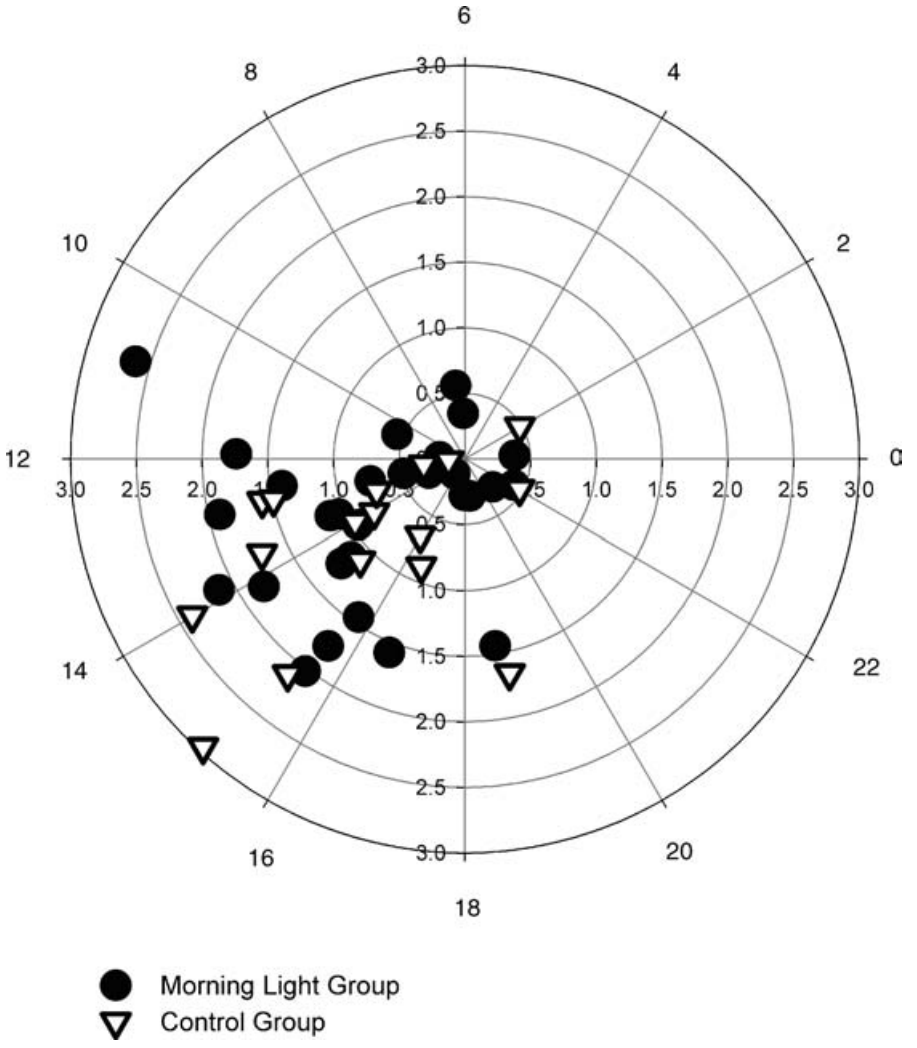

Figure 2. Cosinor-derived activity acrophase (peak) and amplitude at week 11 illustrates persistent between-subjects variability. Position on the angular axis corresponds to clock time, position on the radial axis corresponds to amplitude.

onset times at baseline demonstrated a significant worsening in IV ($p < 0.05$) at the end of intervention compared to baseline. There were no significant improvements in the experimental non-aberrant group or either aberrant or non-aberrant control group subjects.

Similarly, there was a wide variability in M10 onset times at baseline as illustrated in Figure 4, where position on the angular axis again corresponds to clock time. M10 is an indication the rest–activity peak and defined as the 10 most active hours in the 24-hour average curve (Van Someren *et al.*, 1999). Optimal

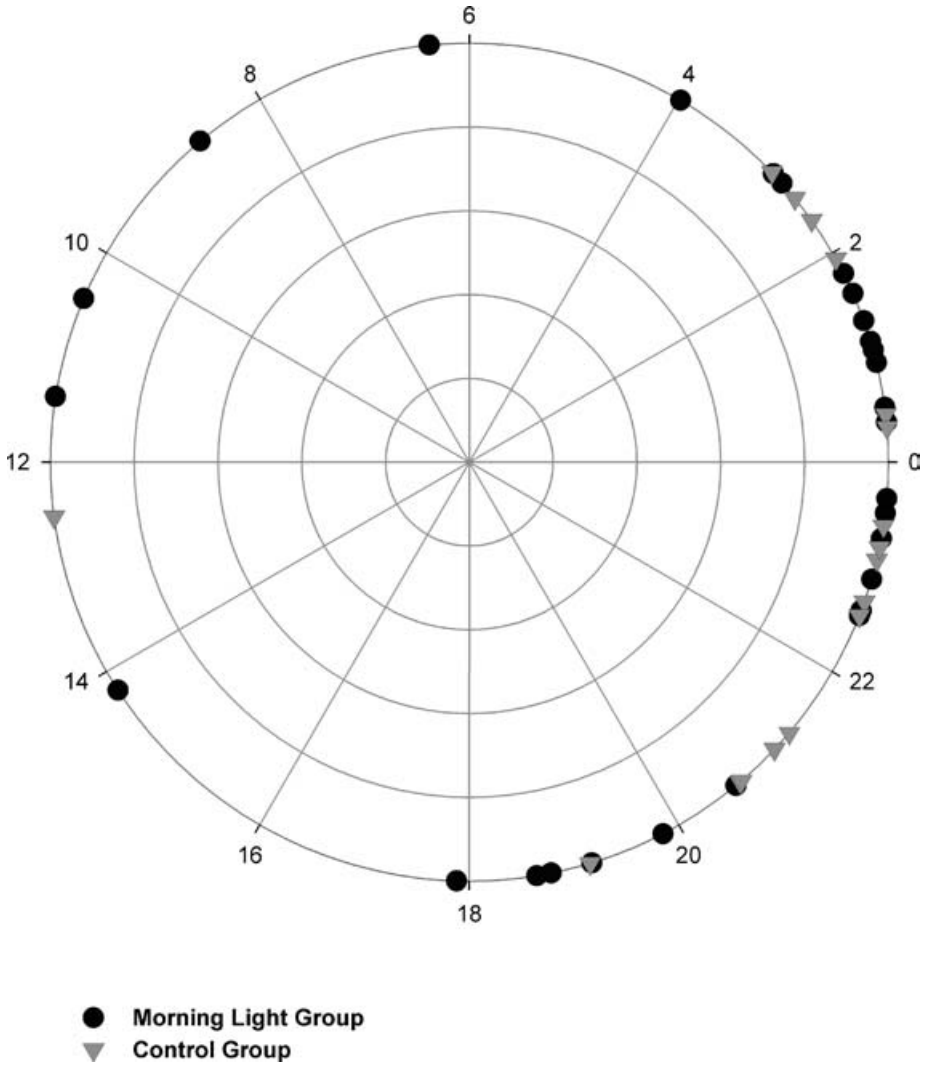

Figure 3. Polar plot illustrates mean time of onset for the five least active hours in the 24-hour day during week 1. Position on the angular axis corresponds to clock time. Onset times between 03:01 and 19:59 are defined as aberrant.

timing of peak activity would be during the day, with possibly some overlap into the 12-hour institutionally defined "night" of 20:00 to 08:00. Subjects were again categorized into two groups based on their M10 onset time. Non-aberrant onset times were defined as those between 06:00 and 12:00 and aberrant times between 12:01 and 05:59. Using this definition, 17 subjects were aberrant ($n = 12$ experimental, $n = 5$ control) and 29 subjects were non-aberrant ($n = 17$ experimental, $n = 12$ control). Seven subjects in the experimental group and

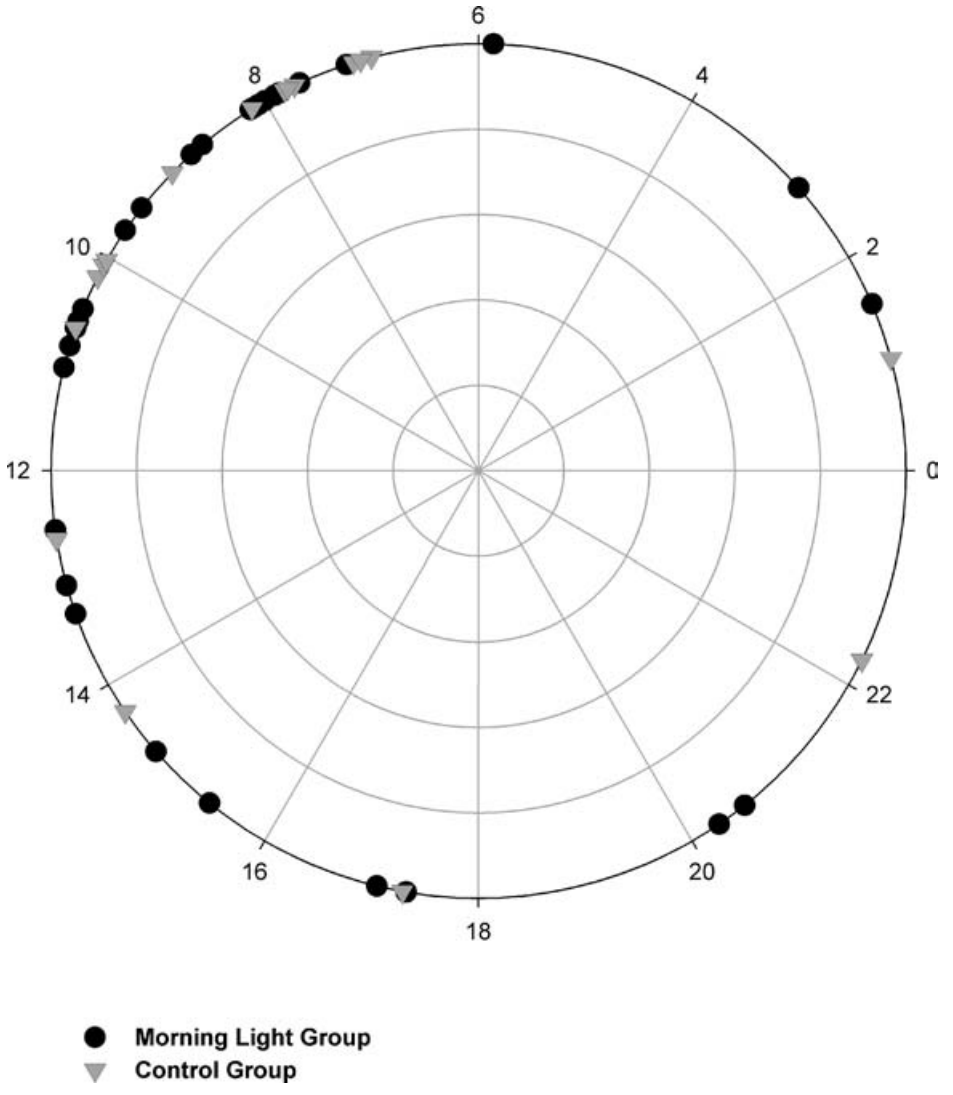

Figure 4. Polar plot illustrates mean time of onset for the 10 most active hours in the 24-hour day during week 1. Position on the angular axis corresponds to clock time. Onset times between 12:01 and 05:59 are defined as aberrant.

two in the control group had both aberrant M10 onset and L5 onset times. Paired *t*-tests on data from subjects in the experimental group with aberrant M10 onset times demonstrated a significant improvement in IS ($p < 0.002$), RA ($p < 0.05$), nighttime sleep efficiency ($p < 0.03$), nighttime sleep time ($p < 0.03$), and nighttime wake time ($p < 0.03$) at the end of intervention compared to baseline. There were no significant improvements in the experimental non-aberrant group or either aberrant or non-aberrant control group subjects.

However, in the control non-aberrant group, there was a trend ($p < 0.06$) toward a decrease in daytime wake time.

Discussion

Our morning bright light exposure protocol did not induce an overall improvement in measures of sleep or the rest–activity rhythm in all experimental as compared to control subjects in the intent-to-treat analyses. Our original purpose in this study was to expose subjects to natural sunlight, but during the course of the study several issues arose. Because of institutional staffing constraints, subjects in the experimental condition were only exposed to bright light Monday through Friday as there was not enough staff to transport the subjects to the bright light condition and engage them in activities to keep them awake with their eyes open on the weekends. It is possible that subjects would have experienced a more robust circadian effect with daily light exposure or exposure of longer duration each day. In addition, there was insufficient natural light on some days to increase the ambient light to our threshold definition of ≥ 2500 lux. We therefore had to supplement the natural light with light boxes to ensure subjects received adequate light exposure.

The most significant improvements were found in the subjects with desynchronized timing of their rest–activity rhythm. Those who experienced their 10 most active hours during the typical hours of sleep at baseline improved their rhythm stability from day-to-day; the difference between their least active and most active periods was strengthened; and sleep efficiency, night sleep and wake times were improved at the end of the intervention.

For both the control and experimental groups, nighttime sleep and daytime wake variables were improved at the week 11 assessment. This observation is consistent with the outcomes of our repeated measures ANOVA, which demonstrated numerous trends or significant main effects of time. Rest–activity disruption was a criteria for inclusion in the study and regression to the mean is very likely to be operating in the data. However, using the randomized pre-post test design with a control group, the regression to the mean phenomena should equally bias experimental and control groups.

The subjects in this study had fairly severe AD with an overall average MMSE score of 6.7 (SD = 6.8, median = 5, range 0–23) and a mean age of 84 years (median = 88, range 60–98). Their rest–activity rhythms were severely disrupted, as reflected by low values for R^2 (mean = 0.12) and stability (mean IS = 0.4), high variability (mean IV = 1.2), and low relative rhythm amplitude (RA = 0.56). In addition, there was significant activity during the defined night as reflected by a high L5 (mean = 54). These findings are similar to those reported by Van Someren and colleagues (1996) in their institutionalized subjects with

dementia who were more impaired on these parameters than control subjects or community dwelling subjects with dementia. Their institutionalized subjects with dementia were also exposed to less light than other subjects and responded to 4 weeks of indirect all-day bright light with increased rhythm stability (Van Someren *et al.*, 1997). Light also significantly improved rhythm stability (IS) in our subjects, who had aberrant L5 onset times at baseline and trended towards strengthening the rest–activity rhythm as evidenced by an increase in RA. Light also resulted in significant improvements in IS and RA in subjects with aberrant M10 onset times at baseline. Furthermore, there was an improvement in nighttime sleep time, nighttime wake time, and sleep efficiency in these subjects. These data suggest that subjects with the most impaired rest–activity rhythms responded positively to the light intervention.

The phase delay of the acrophase of the rest–activity rhythm reported by Ancoli-Israel and colleagues (2002) after exposure of their subjects to morning light was not seen in our sample. However, our subjects had more severe AD (mean MMSE = 6.7) than their subjects (mean MMSE = 12.8) and it is possible that circadian rhythms respond to light differently across the range of cognitive impairment. Our patients with AD were generally poorly entrained to the 24-hour light–dark cycle and tended to phase delay without bright morning light (i.e. control group). Perhaps the experimental group, as a whole, received sufficient additional light to prevent them from phase shifting but not enough to impact other circadian or sleep parameters. And, as described above, the most severely impaired subjects exhibited significant responses.

There was substantial inter- and intraindividual variability in our sample. As noted above, many of our subjects exhibited their 10 most active hours or five least active hours at times other than would be expected based upon the light–dark cycle and institutional routine. It is highly likely that some subjects received the light intervention at an insensitive part of their phase response curve depending on their endogenous time. Or perhaps subjects with dementia have an altered phase response curve to light.

Subjects with the most impaired rest–activity rhythm responded significantly and positively to a one-hour bright light intervention, delivered five days a week for 10 weeks. Bright light remains a potentially promising and practical intervention in the long-term care environment. Further studies are needed to assess whether daily and longer duration of light exposure could produce more robust effects.

Conflict of interest

This work was supported by the National Institutes of Health, National Institute of Nursing Research NR002968, U.S.A. and ZonMW project 2830030 and

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Description of authors' roles

Glenna A. Dowling formulated the research question, designed the study, supervised the data analysis and wrote the manuscript. Jay S. Luxenberg collaborated with Dr. Dowling in formulating the research question, study design, and manuscript writing. Erin M. Hubbard carried out the study intervention, entered and analyzed data, and collaborated on the writing of the manuscript. Judy Mastick assisted in data analysis and writing the manuscript. Robert L. Burr was the principal statistician involved in data analysis and interpretation, and he also contributed to the text of the manuscript. Eus J. W. Van Someren offered his expertise in nonparametric analysis of the data and interpretation, and in writing the manuscript.

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