many risks and disabilities such as Psychiatric disorders and these disabilities are 80% in elderly res-

people will be 60 yr and older by 2050 worldwide

and 26 million in Iran (2-4). Elders are exposed to

idents of nursing homes (5).

**Original Article** 



# Zohre KARAMI<sup>1</sup>, \*Rostam GOLMOHAMMADI<sup>2</sup>, Ahmad HEIDARIPAHLAVIAN<sup>3</sup>, Jalal POOROLAJAL<sup>4</sup>, Rashid HEIDARIMOGHADAM<sup>1</sup>

1. Dept. of Ergonomics, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran

2. Dept. of Ergonomics, School of Public Health AND Research Center for Health Sciences, Hamadan University of Medical

Sciences, Hamadan, Iran

- 3. Dept. of Psychiatry, School of Medicine and Research Center for Behavioral Disorders and Substance Abuse, Hamadan University of Medical Sciences, Hamadan, Iran
- 4. Dept. of Epidemiology and Biostatistics, School of Public Health and Research Center for Health Sciences, Hamadan University of Medical Sciences, Hamadan, Iran

\*Corresponding Author: Email: golmohamadi@umsha.ac.ir

### (Received 04 May 2015; accepted 12 Nov 2015)

### Abstract

Iran J Public Health, Vol. 45, No.5, May 2016, pp.636-643

**Background:** This paper investigated the effect of daylight on morning and night melatonin, subjective general health using GHQ questionnaire, sleepiness and alertness on elderly who lived in nursing houses.

**Methods**: Nineteen nursing home residents participated voluntarily. They exposed to daylight from 9 to 10 a.m. and from 4 to 5 p.m. for 6 wk. The level of melatonin in the morning and at night was measured. General health of all participants was evaluated using General Health Questionnaire (GHQ) as well.

**Results:** Daylight exposure significantly affected morning melatonin from 25.39 pg/ml to 59.77 pg/ml (P=0.001) and night melatonin were changed from 40.30pg/ml to 34.41pg/ml (P=0.081). Mean score of general health changed 36.31 to 29.89 (P=0.003). Karolinska Sleepiness Scale (KSS) and Visual Analogue Scale (VAS) showed increase sleepiness and decrease alertness from 3:00 to 7:00 a.m. Sleepiness decreased and alertness increased during 1:00 p.m. and 20:00 p.m.

**Conclusions:** Daylight exposure could delay sleep phase and correction of circadian rhythm in elderly. Anxiety and insomnia could be improved with daylight exposure. It suggests that elders should be exposed to scheduled daylight in morning and evening for prevention and improvement of mental disorders. Adequate light should be provided for elder's homes and nursing house.

Keywords: Daylight, Melatonin, Health, Circadian rhythm, Elderly, Iran

# Introduction

Elderly population has rapidly been growing in many countries. The prevalence of successful ageing declined steeply from age 70–74 to age 80<sup>+</sup> (1). Two-third of the world's elderly population lives in developing countries such as Iran (2). Life expectancy is increasing, estimated that two billion



Disruption in sleep-wake cycles and melatonin level is one of the important physiological changes in the aging process, which may result in mood disorders and sleep disorders such as decreasing sleep, early morning awakening. Increased level of sleepiness in daytime is common in elders, and inability to stay awake for social events in evening hours (6, 7). Brief morning light treatment for sleep-wake disturbances in old memory-impaired individuals is effective (5, 8, 9). Freidman et al. found exposure to phototherapy diminished sleep in old individuals with memory impairments. Improvement in sleep and mood of caregivers is independent of phototherapy (10). Evening light exposure can increase the amplitude of circadian rhythm, maybe is the cause to delay sleep phase in elders (11). Light improves depression especially of seasonal kind, sleep disorders and most physical and mental disorders (12). Elderly general health in nursing houses especially somatic complain subscale, severe depression, and social dysfunction subscale is low (13). General health subscale such as depression may be affected with Light therapy. Light is available in neutral light outdoors or artificial light forms (14, 15). It may be used as sup-

plementary with antidepressants or alone (in seasonal affective disorders) (16). Light can effect on circadian rhythms through changing in melatonin and circadian rhythms and may have significant effect on sleep-wake cycle (17, 18). It seems exposure to daylight does not have adverse effect (19). We maybe prevent problems caused to elderly persons by taking some measures (12, 20).

The present study was conducted to assess the effect of day light on morning and night melatonin, subjective general health using GHQ questionnaire, sleepiness and alertness on elderly people.

# Methods

### Study design

This before-after clinical trial study was conducted on elderly people who lived in Yase-Sefid and Tolooa nursing houses in Hamadan City, the west of Iran, in 2012. Because limitation of participations we could not use case-control study.

At first, we held meeting in nursing home to describe the objectives and explained how the research would be performed. Then, the eligible subjects voluntarily participated in the study and completed a written informed consent.

The study was approved by Ethics Committee of the Hamadan University of Medical Sciences and was registered by Iranian Registry of Clinical Trials (IRCT201203299014N10).

### **Participants**

Nineteen elders aged 60 to 101 yr; (mean 80±11.27) participated, including twelve females and seven males. Subjects didn't have cognitive disorders. To determine cognitive disorders, we used Mini Mental State Examination (MMSE) and medical history (21). MMSE score below 27 excluded from study.

Inclusion criteria were as follow: (a) age of 60 yr and above; (b) not having acute mental or physical illness; (c) not having of ophthalmological problems; and (c) not having addiction to alcohol and/or narcotic substances. Inclusion criteria of participants were considered by psychiatric physician and study of their history. Cognitive disorders were examined by psychologist used MMSE.

### Illumination condition

The elder's bedroom had insufficient light especially at evening and night. Light intensity was 100 Lux in the bedrooms and 50 Lux in the halls.

### Daily routine

The elders passed in the halls in daytime. The daily routines were same in the nursing homes. According to the nursing home's law the elders waked up at 7:00 a.m. and slept at 22:00 p.m. Time for breakfast, lunch and dinner were the same too. Other activity daily routines were almost same too. The elder's fun was just watching television. In fact, one of our reasons for choosing nursing homes for study was relatively homogeneous conditions.

### Intervention

The intervention of interest was daylight during summer (from August to September) 2012. The intervention determined according to season and light intensity. Light intensity was more than 50

KLux in the horizontal surface and 20 KLux in the vertical surface. If the weather became raining, the participants were exposed to artificial light. There were not any days without intervention. All subjects went outside by investigators and staff every day for the six wk. The participants did not have any interaction with investigators or staff. The participants were exposed to daylight from 9 to 10 a.m. (30 min in this duration) to increase alertness in the morning, and from 4 to 5 p.m. (30 min in this duration) to increase alertness in the evening and delay in sleep phase. Intervention continued 6 wk. The sun light at that duration was suitable and it was not annoying at that duration. The artificial light used in previous studies was 10000 Lux in 30 min, so 30 min intervention in our study was enough according to sun light intensity. The participants were asked if any adverse effect informed researchers. All subjects went outside every day for the six week and we did not use artificial light.

### Assessment procedure

Two blood samples (5cc) were taken at 7:00 a.m. After waking up and 8:00 p.m. samples were taken before and after treatment period to assess melatonin level.

the samples were Centrifuged for 1 min at 500 xg, Cover tubes Incubate 16-24 h at RT (18-25 °C), Pipette 500  $\mu$ L of Precipitating Antiserum into each tube Incubate 15 min at RT (18-25 °C), Centrifuge all tubes for 15 min at 3000 xg. The temperature of the rotor should not exceed 25 °C, Decant all tubes in overhead position for 3-5 min, Count the tubes in a Gamma counter for 1 min.

The General Health Questionnaire (GHQ) is a screening device for identifying minor psychiatric disorders in the general population that within community or non-psychiatric clinical settings such as care or general medical out-patients. The 28-item General Health Questionnaire (GHQ–28) is a self-administered method to quantify the risk of developing psychiatric disorders. This instrument targets two areas – the inability to perform functions and the appearance of distress – to assess well-being in a person (22). The questionnaire evaluates somatic complain, severe depression,

anxiety and insomnia and social dysfunction. This questionnaire was developed by Goldberg & Hillier and has been widely used in many countries in clinical and mental disorders (23). The reported Cronbach alpha coefficient for the GHQ was a range of 0.82 to 0.86 (23, 24). We used this questionnaire for the elders that had normal cognition and didn't have acute mental disorders filled out the questionnaire. Maximum score is 84 in GHQ and is 21 in subscales and higher score indicates worsen wellbeing (25).

Visual analogue scale (VAS) was used as a psychometric response scale to assess fatigue and alertness of elders (26). The measurement tool was a 10 cm ruler in which number zero means minimum fatigue and maximum alertness and number 10 meant maximum fatigue and minimum alertness. Participants were asked to mark their fatigue and alertness in past 24 h. We told to the participants about VAS and KSS scale one day before evaluation. It was taken once at baseline and once after the treatment period.

The Karolinska Sleepiness Scale (KSS) which is a 9-point Likert scale was used for evaluating subjective sleepiness; 1=extremely alert, 2=very alert, 3=alert, 4=rather alert, 5=neither alert nor sleepy, 6=some signs of sleepiness, 7=sleepy, no effort to stay awake, 8=sleepy, some effort to stay awake, 9=very sleepy, great effort to keep awake, fighting sleep, 10 meant participant was in deep sleep and individuals could not attempt to be awake. Participants were asked to rate their level of sleepiness in the past 24 hours. It was given once at baseline and once after the treatment period (27). We could estimate circadian shifting used comparison of melatonin level with VAS rational and KSS rational before and after intervention.

The intervention group was selected in nursing house residents, so we could control some factors associated with the intervention that caused the change in melatonin, VAS, KSS, and GHQ scores.

### Statistical Analysis

Chi-square test was used for comparison of nominal variables, and *t*-test for quantitative variables, All statistical analyses were performed at the 95% significance level using the statistical software Stata version 11.2 (StataCorp, College Station, TX).

### Results

### Melatonin level

The mean melatonin level was  $25.39(\pm 19.74)$  pg/ml before intervention at 7:00 a.m., and  $59.77(\pm 41.78)$  pg/ml after intervention (*P*=0.001) (Table 1). Night melatonin did not have statistical difference (*P*=0.081) (Table 1). Comparison Table 1 with Fig.1 shows day light exposure can correct sleep disturbance and delay sleep phase in elders.



Fig. 1: Level of fatigue using Visual Analog Scale (VAS)

 Table 1: Mean concentration of melatonin (pg/ml) in the morning and night before and after intervention using paired *t*-test

Mean concentration of melatonin (pg/ml)	Ν	Mean	SD	<b>P</b> Value
Mean melatonin 7 a.m.:	-			
Before intervention	19	25.39	19.74	0.001
After intervention	19	59.77	41.78	
Mean melatonin 8 p.m.:				
Before intervention	19	40.30	21.55	0.081
After intervention	19	34.41	16.60	

### General health

The subscales score improved from sever disturbances to moderate and mild disturbances. This table shows that mean score of GHQ before intervention was  $36.31(\pm 12.75)$ . After intervention mean score of GHQ changed 36.31 to  $29.89(\pm 10.69)$  (*P*=0.003) (Table 2). The mean somatic complain was 8.05 ( $\pm 4.49$ ) before intervention, it decreased to  $6.78(\pm 2.74)$  after intervention

(P=0.072); The mean anxiety was 8.42 (±3.28) before intervention, it decreased to 5.68(±2.76) after intervention (P=0.001); The mean social dysfunction score was 13.15(±3.30) before intervention, it decreased to 12.10(±3.91) after intervention (P=0.209); The mean depression score was 6.26(±3.75) before intervention, it decreased to 5.31(±3.40) after intervention (P=0.107) (Table 2).

Table 2: Mean score of general health questionnaire (GHQ) before and after intervention using paired *t*-test

Mean score of GHQ	Ν	Mean	SD	<b>P</b> value
Total before intervention	19	36.31	12.75	0.003
Total after intervention	19	29.89	10.69	
Somatic before intervention	19	8.05	4.49	0.072
Somatic after intervention	19	6.78	2.74	
Anxiety/insomnia before intervention	19	8.42	3.28	0.001
Anxiety/insomnia after intervention	19	5.68	2.76	
Social before intervention	19	13.15	3.30	0.209
Social after intervention	19	12.10	3.91	
Depression before intervention	19	6.26	3.75	0.107
Depression after intervention	19	5.31	3.40	

There was significant difference in anxiety and insomnia after intervention, but there was not seen significantly difference in somatic complain, social dysfunction and severe depression.

### Sleepiness

Sleepiness at night was disturbed from 2:00 a.m. to 7:00 a.m. before intervention. During 1:00 a.m. to 7:00 a.m. Sleepiness was increased from 7.45( $\pm$ 1.29) before intervention to 8.67( $\pm$ 1.10) after intervention (*P*=0.01). During 8:00 a.m. to 12:00 a.m. sleepiness decreased from 2.77( $\pm$ 1.61)

before intervention to  $2.42(\pm 1.50)$  after intervention (P=0.04). During 1:00 p.m. to 7:00 p.m., sleepiness decreased from 5.67( $\pm 2.07$ ) before intervention to  $3.99(\pm 1.76)$  after intervention. Alertness was increased from 8:00 a.m. to 8:00 p.m after intervention. All participants improved in night sleep quality and daytime alertness after intervention (Table 3). Comparison Table 1 with Table 2 and Table 3 shows daylight exposure can correct sleep disturbance and delay sleep phase in elders.

 Table 3: Level of sleepiness using Karolinska Sleepiness Scale (KSS)

Hours	Ν	Mean	SD	<b>P</b> value
1:00 a.m. to 7:00 a.m. before	19	7.65	1.29	0.01
1:00 a.m.to 7:00 a.m. after		8.67	1.10	
8:00 a.m. to 12:00 a.m. before	19	2.77	1.61	0.04
8:00 a.m. to 12:00 a.m. after		2.42	1.50	
1:00 p.m. to 7:00 p.m. before	19	5.67	2.07	0.03
1:00 a.m. to 7:00 p.m. after		3.99	1.76	
8:00 p.m. to 12:00 p.m. before	19	7.54	1.62	0.95
8:00 p.m. to 12:00 p.m. after		7.56	0.93	

### Fatigue and alertness

The results of day-night trend of fatigue using Visual Analog Scale (VAS) in Fig. 1 showed the after/before intervention levels between 8 p.m. to 12 p.m. increasing from 5.99 ( $\pm$ 1.86) to 6.77( $\pm$ 2.18) (*P*=0.17) and 1 a.m. to 7 a.m. from 7.83( $\pm$ 1.20) to 8.51( $\pm$ 1) (*P*=0.04), also fatigue scale reduced between 7 a.m. to 12 a.m. from 2.95 ( $\pm$ 1.99) to 2.50 ( $\pm$ 1.33) (*P*= 0.46) and 1 p.m. to 7 p.m. from 4.91( $\pm$ 2.14) to 3.75( $\pm$ 1.68) (*P*=0.05).

# Discussion

This before-after clinical trial study was done with aim of investigation of daylight on melatonin level and subjective general health that it seems successful. The light deprivation is one of the causes for disturbance in circadian rhythm (11). Evening sleepiness is one of the major complications among elders, as mean sleepiness in daytime was decreased 0.89 score. The elder's sleepiness was compared at 20-min (group 1) versus 45-min (group 2) by Kirisoglu and Guilleminault. The VAS mean in group 1 was decreased 2.32 score after 3 month and 1.76 score after 6 mo; VAS mean in group 2 was decreased 2.63 score after 3 mo and 2.6 score after 6 mo (28). The prevalence of psychiatric disorders in elderly

residents of nursing houses is high (13, 29). General health in the elders is too low (29). In this study GHQ scores was 36.31 at baseline. The results of previous studies showed GHQ score was 30.05 and 44.14 (13, 29). Somatic complains score was 3.47, anxiety and sleepiness score was 8.34, social dysfunction score was 8.50 and severe depression score was 9.74 (13). In this study somatic complain score is 8.05, anxiety and sleepiness score is 8.42, social dysfunction score is 13.15 and severe depression score is 6.26. The comparison of these studies indicates our participants were in better condition. General health improved after intervention. This study indicates

daylight intervention could be effective in elder's general health especially in anxiety and sleepiness. This continuous character of VAS scale differentiates it from discrete scales, such as the Likert scale. "There is evidence that shows the visual analogue scales have superior metrical characteristics than discrete scales, therefore, a wider range of statistical methods can be applied to the measurements" (26). The influence of Bright Light on sleep parameters was examined on the Hospitalized Elderly patients by Wakamura and Tokura. They found that bright light exposure improved sleeping in hospitalized elderly patients. The average of salivary melatonin concentration at midnight was increased in four patients of seven from  $7.5\pm2.6$  pg/ml to  $13.3\pm9.2$  pg/ml (30). Friedman et al found that an increase in bright light exposure is only effective in older adults with a specific deficit in their circadian system. They concluded improvement in sleep may be due to participation in this protocol or the sleep hygiene therapy (10). But our results showed that day light exposure improved sleep in elders. Van Somern et al concluded that bright light therapy is effective for sleep/wake rhythm disorders (31). They used actigraphy to assess effect of indirect bright light on rest-activity rhythm disturbances in demented patients. They found that the "stability of the rest-activity rhythm" increased during increased illumination in patients with "intact vision, but not in visually impaired patients" (15).

# Conclusion

Overall daylight exposure could delay sleep phase in elders. Sleep disorders especially sleepiness at evening and waking at midnight in elders could correct. Sleepiness, fatigue and alertness at day time may be improved. Subjective general health, especially anxiety and insomnia, could be improved with daylight exposure. Our findings suggest that elders should be exposed to scheduled daylight in morning and evening for prevention of mental disorders and sleep disorders. Adequate neutral light should be provided for elder's homes and nursing houses for prevention and even improvement of elderly problems. More studies and researches will be useful especially in evening light exposure. We suggest that future studies should be done with case and control. Melatonin assessment should be measured in evening, not during night, in order to show alertness and sleepiness at evening. Combination of daylight exposure with daily activity and interesting sport activities should be studied.

# Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

# Acknowledgments

We thank the Vice-Chancellor of Education and the Vice-Chancellor of Research and Technology, Hamadan University of Medical Sciences, which approved this study. Also we would like to thank the directors, residents and staffs of Yase-Sefid and Tolooa nursing houses for their collaboration with this study. This article was a part of MSc thesis in occupational health funded by Hamadan University of Medical Sciences. Authors have no conflicts of interests to disclose.

# References

- Jorm AF, Christensen H, Henderson AS, Jacomb PA, Korten AE, Mackinnon A (1998). Factors associated with successful ageing. *Australas J Ageing*, 17:33-37.
- 2. WHO . Aging and life course. 2009 [cited 10 September 2009; Available from: http://www.who.int/ageing/en/.
- Booth H, Tickle L (2003). The future aged: new projections of Australia.'s elderly population. *Australas J Ageing*, 22(4):196-202.
- Jimison H, Pavel M, McKanna J, Pavel J (2004). Unobtrusive monitoring of computer interactions to detect cognitive status in

elders. IEEE Trans Inf Technol Biomed, 8:248-252.

- Chesson A, Littner M, Davila D, Anderson WM, Grigg-Damberger M, Hartse K, Johnson S, Wise M (1999). Practice parameters for the use of light therapy in the treatment of sleep disorders. *Sleep*, 22:641-660.
- 6. Deschenes CL, McCurry SM (2009). Current treatments for sleep disturbances in individuals with dementia. *Curr Psychiatry Rep*, 11(1):20-26.
- Galimi R (2010). Insomnia in the elderly: an update and future challenges. G Gerontol, 58:231-247.
- 8. Forbes D, Morgan DG, Bangma J, Peacock S, Pelletier N, Adamson J (2004). Light therapy for managing sleep, behaviour, and mood disturbances in dementia. *Cochrane Database Syst Rev*, (2):CD003946.
- Ancoli-Israel S, Gehrman P, Martin JL, Shochat T, Marler M, Corey-Bloom J, Levi L (2003). Increased light exposure consolidates sleep and strengthens circadian rhythms in severe Alzheimer's disease patients. *Behav Sleep Med*, 1:22-36.
- Friedman L, Spira AP, Hernandez B, Mather C, Sheikh J, Ancoli-Israel S, Yesavage JA, Zeitzer JM (2012). Brief morning light treatment for sleep/wake disturbances in older memoryimpaired individuals and their caregivers. *Sleep med*, 13:546-549.
- Shirani A, Louis EKS (2009). Illuminating rationale and uses for light therapy. J Clin Sleep Med, 5:155-163.
- Dowling GA, Burr RL, Van Someren EJ, Hubbard EM, Luxenberg JS, Mastick J, Cooper BA (2008). Melatonin and Bright-Light Treatment for Rest–Activity Disruption in Institutionalized Patients with Alzheimer's Disease. J Am Geriatr Soc, 56:239-246.
- Momeni K, Karimi H (2011). Comparison of mental health between elderly admitted in sanitarium with elderly in sited in personal home. J Kermanshah Univ Med Sci, 14(4): 328-335.
- Hahn IH, Grynderup MB, Dalsgaard SB, et al. (2011). Does outdoor work during the winter season protect against depression and mood difficulties? *Scand J Work Emiron Health*, 37(5):446-9.

- Van Someren EJ, Kessler A, Mirmiran M, Swaab DF (1997). Indirect bright light improves circadian rest-activity rhythm disturbances in demented patients. *Biol Psychiatry*, 41:955-963.
- 16. Eagles JM (2009). Light therapy and seasonal affective disorder. *Psychiatry*, 8:125-129.
- Campbell SS, Dijk DJ, Boulos Z, Eastman CI, Lewy AJ, Terman M (1995). Light treatment for sleep disorders: consensus report III. Alerting and activating effects. J Biol Rhythms, 10:129-132.
- Yamadera H, Ito T, Suzuki H, Asayama K, Ito R, Endo S (2000). Effects of bright light on cognitive and sleep–wake (circadian) rhythm disturbances in Alzheimer-type dementia. *Psychiatry Clin Neurosci*, 54:352-353.
- 19. Terman M, Terman JS (1999). Bright light therapy: side effects and benefits across the symptom spectrum. J Clin Psychiatry, 60:799-808.
- Kohsaka M, Fukuda N, Kobayashi R, Honma H, Sakakibara S, Koyama E, Nakano O, Matsubara H (1998). Effects of short duration morning bright light in healthy elderly. II: Sleep and motor activity. *Psychiatry Clin Neurosci*, 52:252-253.
- Tiwari S, Tripathi RK, Kumar A (2009). Applicability of the Mini-mental State Examination (MMSE) and the Hindi Mental State Examination (HMSE) to the urban elderly in India: a pilot study. *Int Psychogeriatr*, 21:123-128.
- 22. Goldberg D, Williams P (2000). General health questionnaire (GHQ). *Swindon, Wiltshire, UK: nferNelson.*
- 23. Jackson C (2007). The general health questionnaire. Occup Med, 57:79.
- 24. Taghavi MR (2008). The normalization of General Health Questionnaire for shiraz university student (GHQ-28). *CPAP*, 1(28):1-12.
- 25. Vallejo MA, Jordán CM, Díaz MI, Comeche MI, Ortega J (2007). Psychological assessment via the internet: a reliability and validity study of online (vs paper-and-pencil) versions of the General Health Questionnaire-28 (GHQ-28) and the Symptoms Check-List-90-Revised (SCL-90-R). J Med Internet Res, 9(1): e2.
- Phan NQ, Blome C, Fritz F, Gerss J, Reich A, Ebata T, Augustin M, Szepietowski JC, Ständer S (2012). Assessment of pruritus

intensity: prospective study on validity and reliability of the visual analogue scale, numerical rating scale and verbal rating scale in 471 patients with chronic pruritus. *Acta Derm Venereol*, 92:502-507.

- 27. Kaida K, Takahashi M, Åkerstedt T, Nakata A, Otsuka Y, Haratani T, Fukasawa K (2006). Validation of the Karolinska sleepiness scale against performance and EEG variables. *Clin Neurophysiol*, 117:1574-1581.
- Kirisoglu C, Guilleminault C (2004). Twenty minutes versus forty-five minutes morning bright light treatment on sleep onset insomnia in elderly subjects. J Psychosom Res, 56:537-542.

- 29. Pasha G, Safarzade S, Mashak R (2008). Comparison betweenhealth and social support among the elderly in nursing homes and family. *Famili Research*, 3:503-17.
- Wakamura T, Tokura H (2001). Influence of bright light during daytime on sleep parameters in hospitalized elderly patients. J Physiol Anthropol Appl Human Sci, 20:345-351.
- 31. Van Someren EJ, Swaab DF, Colenda CC, Cohen W, McCall WV, Rosenquist PB (1999). Bright light therapy: improved sensitivity to its effects on rest-activity rhythms in Alzheimer patients by application of nonparametric methods. *Chronobiol Int*, 16:505-518.