A Follow-Up Study of Actigraphic Measures in Home-Residing Alzheimer's Disease Patients

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ABSTRACT

This article reports cross-sectional and follow-up data with actigraphic measures of nocturnal sleep and rest/activity in 61 Alzheimer's disease (AD) patients as well as the relation of actigraphic measures to levels of behavioral disturbance across different stages of the disease. Over the course of approximately 1.5 years' follow-up, patients showed significant deterioration of nocturnal sleep parameters, but no significant change in rest/activity circadian rhythm parameters. There were also significant correlations among nocturnal sleep, rest/activity circadian rhythm, and behavioral disturbance measures, but only in relatively early stages of AD. It is argued that study of nocturnal sleep and circadian rhythm in relation to behavioral disturbance in AD requires longitudinal data and analyses that take into account the stage of disease at which patients are assessed. (*J Geriatr Psychiatry Neurol* 1998; 11:7–10).

Nocturnal sleep disruption is reported to be a major problem for the families of Alzheimer's disease (AD) patients and is often cited as a reason for institutionalization.[1,2] A growing number of cross-sectional studies have used actigraphic monitoring to measure rest/activity circadian rhythms and/or sleep/wake in AD patients,[3–13] but none of these studies has followed AD patients over time. The purpose of this paper is to present follow-up actigraphic data on AD patients. Furthermore, the data will be presented in relation to overall levels of behavioral disturbance across different stages of the disease.

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METHODS

Subjects

All patients whose data are presented in this report had a diagnosis of probable AD by NINCDS-ADRDA criteria[14] at entry into a longitudinal study of AD at the Stanford Aging Clinical Research Center (ACRC). Patients were followed at approximately 6-month intervals and were living at home during the period of study. We report on observations for 61 subjects, of whom 57% were men. Subjects' average age at first actigraphic testing was 71.4 years (SD = 8.1, range 51–86 years) and they had a mean Mini-Mental State Examination (MMSE)[15] score of 17.6 (SD = 6.0) at this time. Data from some of the current subjects have been included in previous papers at earlier stages of this longitudinal study.[5,16,17]

Measures

Mini-Mental State Examination

The 30-item MMSE measures cognitive abilities known to decline with AD. Scores range from 30–0 with lower scores indicating greater impairment. Recently, MMSE scores have been grouped into stages to create clinically identifiable levels of severity of AD: 1 (Early: MMSE = 24–30); 2 (Mild: MMSE = 15–23); 3 (Moderate: MMSE

= 8–14); 4 (Moderately Severe: MMSE = 4–7); 5 (Severe: MMSE = 0–3).[18]

Time-Based Behavioral Disturbance Questionnaire

In the time-based behavioral disturbance questionnaire (TBDQ), caregivers report whether, over the previous month, a patient exhibited any of seven behaviors (combativeness, agitation, wandering, incoherent speech, hallucinations, confusion, and disorientation) in any of four periods of the day: morning, early afternoon, late afternoon/evening, and night. An "overall" score was computed for each TBDQ observation equal to the fraction of the seven behaviors that occurred across the 24-hour day. This score can range from 0.0 to 1.0.

Actigraph

The actigraph is an ambulatory motion-detecting device (Ambulatory Monitoring Systems, Inc., Ardsley, NY 10502). Patients wore actigraphs on their nondominant wrists 24 hours a day for periods of approximately 6 days. Movement data were collected in 30-second epochs. The actigraph was removed primarily for activities that would cause it to be submerged in water.

Calculation of Circadian Activity Measures from Actigraph Data

Measures of rest/activity circadian rhythm were obtained from the actigraph data by using a least-squares method to compute a multiple correlation coefficient (r^2) measure of goodness of fit to a cosine curve. In addition, the mesor (mean activity level), amplitude, and acrophase (peak time) were computed. These measures were validated by comparisons with rhythm amplitude estimates from raw data waveforms. Data were available on 61 subjects: 23 of whom had one datapoint; 17 had two datapoints; 11 had three datapoints; and 10 had four or more datapoints.

Calculation of Nocturnal Sleep Measures from Actigraph Data

The actigraph recordings were also computer-scored to determine nocturnal sleep parameters with the program, ACTION 1.3 (Ambulatory Monitoring Systems). The program requires entry of subjects' bed times and final morning out-of-bed times and this information was taken from sleep logs completed by caregivers for each 24-hour period of actigraph recordings. The program quantifies the motion data into the following sleep parameters: the amount of time spent in bed during the night sleep period (TIB), time to sleep onset at the beginning of the sleep period (SO), total time spent in sleep during the sleep period (TST), the amount of time awake after sleep onset (WASO), and sleep efficiency (SE), which is the percentage of time in bed spent actually sleeping or (TST/TIB) × 100.

Reported reliabilities of actigraphically scored total sleep time (TST) compared with polysomnographic recordings have ranged from +.98 in 5 normal subjects[19] to +.84 in 25 sleep apnea subjects.[20] A recent study found actigraphically determined sleep to correlate from .81 to .91 with polysomnography (depending on whether the intensity or frequency of movement was measured) in a sample of institutionalized AD patients.[21] In our study, actigraphic sleep data were available for 49 subjects: 18 of whom had one datapoint; 19 had two datapoints; 5 had three datapoints; and 7 had four or more datapoints.

RESULTS

Table 1 presents a summary of cross-sectional data on actigraphic measures by MMSE stage of illness. To present the maximum amount of cross-sectional data, note that we included data in Table 1 for all patients for whom we had actigraphic recordings in each MMSE stage. We were able to score for nocturnal sleep only those actigraphic data for which we had accompanying sleep

Table 1. Summary Cross-Sectional Data on Actigraphic Measures by Stage of Illness

	MMSE Stage			
	1	*2*	*3*	*4–5*
Sleep/Wake (103 observations)				
n	19	42	30	12
TIB (min)	532.7 (52.4)	554.9 (106.6)	564.9 (72.2)	584.2 (116.8)
TST (min)	409.7 (77.4)	406.9 (95.9)	420.0 (100.2)	427.2 (107.4)
SE (%)	77.3 (13.9)	73.8 (12.6)	74.1 (14.8)	73.3 (13.9)
SO (min)	17.1 (11.5)	18.9 (15.7)	20.6 (15.0)	25.6 (15.9)
WASO (min)	95.8 (80.7)	106.5 (67.8)	109.6 (73.1)	112.6 (65.9)
Circadian Rhythm (137 observations)				
n	27	55	36	19
Mesor	59.3 (15.2)	57.2 (13.0)	59.9 (12.4)	62.6 (8.9)
Amplitude	41.3 (12.6)	39.9 (11.6)	41.8 (13.9)	45.8 (10.7)
Acrophase	16.0 (1.4)	15.0 (1.0)	15.3 (1.0)	15.1 (1.3)
r^2	0.65 (0.21)	0.60 (0.20)	0.61 (0.20)	0.70 (0.10)

All available measurements are used in this Table; standard deviation in parentheses.

Table 2. Summary Follow-up Data on Actigraphic Measures

	Mean	SD	Mean Change	SD	t	P
Sleep/Wake (n = 29)						
Duration of Follow-up (days)	479	275				
Initial MMSE	17.7	5.3				
MMSE			−4.5	4.3		
TIB (min)			42.5	80.3	2.85	.008
TST (min)			−12.7	76.2	−.90	.38
SE (%)			−8.0	12.9	−3.33	.002
SO (min)			8.5	17.4	2.62	.01
WASO (min)			40.8	65.2	3.37	.002
Circadian Rhythm (n=36)						
Duration of Follow-up (days)	604	336				
Initial MMSE	18.4	6.1				
MMSE			−5.6	5.0		
Mesor			3.9	13.2	1.77	.09
Amplitude			0.8	12.9	.39	.70
Acrophase			−.05	1.14	−.24	.81
r^2			.02	.24	.44	.66

Individual patients were followed for at least 6 months.

logs. Thus there are 103 recordings scored for nocturnal sleep, although there were 137 available for rest/activity circadian rhythm scoring. In Table 2, data are presented for those patients for whom we had repeated recordings and whom we followed for at least 6 months. There were follow-up sleep/wake data for 29 patients and follow-up rest/activity circadian rhythm data for 36 patients who met this criterion. In cases for which more than two recordings were available, difference scores were calculated using data from the recording sessions that were the maximum time apart. We also calculated *t*-tests to determine if a significant change in each variable had occurred over time.

We next calculated correlation coefficients between actigraphically derived measures of nocturnal sleep and rest/activity circadian rhythm and the corresponding overall TBDQ scores for each patient within stages of AD. In patients in the initial stages of AD, i.e., MMSE Stages 1 and 2 combined, the Spearman correlation between the TBDQ and SE was −.45 (n = 28, P = .02), between the TBDQ and SO, .44 (n = 28, P = .02), and between the TBDQ and WASO, .46 (n = 28, P = .02). Regarding rest/activity circadian rhythm variables from patients in MMSE Stages 1 and 2, the correlation between the TBDQ and amplitude was −.40 (n = 38, P = .02); however, neither the correlation between the TBDQ and acrophase nor between the TBDQ and mesor was significant. In Stage 3, no correlations between the TBDQ and any nocturnal sleep or rest/activity circadian rhythm measures were significant (n = 20 for circadian measures and n = 18 for sleep measures). Finally, combining subjects in MMSE Stages 4 and 5 again showed that no correlations between the TBDQ and any nocturnal sleep or rest/activity circadian rhythm measures were significant (n = 11 for circadian measures and n = 8 for sleep measures).

DISCUSSION

The actigraphically derived nocturnal sleep parameters in our AD patients appear to be different from published polysomnographic data on normal older populations. Averaging the reported findings of several EEG studies of normal elderly subjects with a mean age of 70.4 years[22–24] produced the following mean values: TIB, 443.0 min; TST, 365.3 min; SE, 83%; SO, 22.2 min; and WASO, 55.3 min.

There are few studies reporting actigraphically recorded sleep in normal elderly. Aharon-Peretz et al[3] reported actigraphic nocturnal sleep with SE, 82% and TST, 444 min in a group of healthy older control subjects (mean age = 69 years) whose sleep did not differ significantly from a sample of early stage AD patients (72.8 years). Evans and Rogers[25] reported TIB, 460 min; TST, 375 min; SE, 81%; SO, 13 min; and WASO, 63 min in a group of healthy old-old adults (mean age = 81.2 years). Our MMSE Stage 1 AD patients had averages of TIB, 533 min; TST, 410 min; SE, 77%; SO, 17 min; and WASO, 96 min. Our MMSE Stage 3 patients, on the other hand, had on average: TIB, 565 min; TST, 420 min; SE, 74%; SO, 21 min; and WASO, 110 min. Thus the major difference between the AD patients' sleep and that of the normal older individuals was lower sleep efficiency; the AD patients spent a longer period of time in bed at night and had a longer wake time after sleep onset. Similar to findings on EEG recorded sleep in AD patients, sleep characteristics in our patients appeared to worsen with progression of the illness.[26]

In both the follow-up and cross-sectional data for our patients there was a more noticeable deterioration of sleep than of the circadian rhythm indices over a follow-up period that averaged 1.5 years. By way of comparison, although Hoch et al[27] found no significant differences over a 3-year follow-up in EEG-measured sleep variables of SE, SO, and WASO in healthy young-old adults (61–74 years), there were significant negative changes in these variables in healthy old-old adults (75–87 years). Over a shorter time period, the sleep of our AD patients with a mean age of 71.4 years at first testing displayed deterioration similar to that of the healthy old-old individuals who had a mean age of 81.1 years.

Regarding rest/activity measures, previous studies using the actigraph have found increased nocturnal activity in AD patients relative to normal controls[9] and relative to earlier stages of the disease.[7] Progressive decrease in the rest/activity circadian rhythm has been found with increasing duration of illness or stage of disease.[4,6] Pollak and Stokes[8] did not find any differences between nocturnal activity of home-dwelling dementia patients and their caregivers, although they found that the dementia patients were significantly less active in the day.

Our own follow-up data do not show any significant changes in rest/activity circadian rhythm parameters in 36 subjects followed for an average of approximately 1.5 years. Continued study of these patients may document significant changes over longer periods of follow-up; however, the magnitude of the circadian rhythm changes appears to be smaller than the magnitude of the changes in the nocturnal sleep parameters that reached statistical significance with fewer subjects followed for approximately the same period of time. We note that few subjects have as yet been followed into MMSE Stages 4 and 5; hence, they may yet show deterioration of rest/activity circadian rhythm function.

We have data primarily from patients in the earlier stages of the disease and the n available in each stage is relatively small. Nonetheless, our preliminary behavioral data suggests, as it has in the past,[5] that in MMSE Stages 1 and 2 those patients with poor nocturnal sleep have greater behavioral disturbance. However, these correlations seem to disappear in later stages of the disease. Although many have criticized staging schema,[18] this has implications for other studies, because if subjects in a cross-sectional study are sampled from different stages, the resulting correlation coefficient will mix subjects from different stages across correlations. We believe that this may be a significant source of inconsistent findings across studies and that it is essential to account for the stage of illness when evaluating relations among behavioral disturbance and sleep and circadian rhythm measures in AD patients.[28] In our own work, a continuing longitudinal study of the same patients will be necessary to draw definitive conclusions about the course of circadian rhythm and nocturnal sleep disturbances in AD as well as relations between nocturnal sleep and rest/activity circadian rhythm disturbances and behavioral disturbances at different stages of AD.

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