

# Disruptive Behavior and Actigraphic Measures in Home-Dwelling Patients with Alzheimer's Disease: Preliminary Report

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## ABSTRACT

The purpose of this preliminary report was to explore overall level and diurnal patterning of caregiver reports of abnormal behavior and to explore relationships with actigraphic measures of sleep/wake activity in Alzheimer's disease (AD) patients. Our primary behavioral measure was the Time-based Behavioral Disturbance Questionnaire (TBDQ). The overall score on this measure was shown to have adequate test-retest reliability and convergent validity with another behavioral measure. Significant correlations were obtained between the TBDQ overall score and actigraphically scored sleep efficiency ( $r = -.35, P < .05$ ) and wake after sleep onset ( $r = .43, P < .01$ ) in 41 subjects. The data suggest a moderate relationship between actigraphic measures of sleep/wake and disturbed behavior in home-dwelling AD patients. (*J Geriatr Psychiatry Neurol* 1997; 10:58-62).

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The purpose of this preliminary report was to explore the overall level and diurnal patterning of caregiver reports of abnormal behavior and to explore relationships of reported abnormal behavior with actigraphic measures of sleep/wake activity in Alzheimer's disease (AD) patients. Using self-report measures, Ancoli-Israel and associates<sup>1</sup> suggested that sleep disturbances may be associated with increased behavioral disturbance in AD patients. Using measures of core-body temperature and locomotor activity, Satlin and associates<sup>2</sup> suggested that a subgroup of AD patients have impaired endogenous circadian-rhythm pacemaker function that is linked to fragmented nocturnal sleep. Data, however, are not yet available linking behavioral disturbance measures with actigraphic or polysomnographic objective measures of sleep/wake activity in AD patients.

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## METHODS

### Subjects

All patients in this report had a diagnosis of probable AD by NINCDS-ADRDA criteria<sup>3</sup> at entry into a longitudinal study of AD at the Stanford University Aging Clinical Research Center (ACRC). All were living at home during the study. Patients' behavior was followed at intervals of approximately 6 months. We report on a total of 169 observations for 101 subjects (69 males, 32 females). The mean age of the subjects was  $70 \pm 6.9$  (SD) years old (range, 56-88 yr) and they had a mean Mini-Mental State Examination (MMSE)<sup>4</sup> score of  $15.8 \pm 8.2$  at the time the caregiver completed the first Time-based Behavioral Disturbance Questionnaire (TBDQ).<sup>5</sup> Subjects' mean age at reported onset of AD was  $64.2 \pm 6.8$  years, with a range of 50 to 91 years. There were 59 patients for whom we had one observation, 24 with two, 12 with three, 4 for four, and 2 with five observations. Of these, 90 patients (135 observations) had MMSE determination concurrent with the TBDQ. The majority (91/101) of caregivers were spouses; nine were offspring, and one was another relative. Some of the current subjects have been included in previous papers written when there were fewer observations and no longitudinal data analyzed.<sup>5,6</sup>

## Measures

### Age at Disease Onset

This was based on caregivers' recall in the initial structured interview at entry to the longitudinal study.

### The Mini-Mental State Examination

The MMSE<sup>4</sup> is a commonly used measure of general mental status. It consists of 30 items that measure abilities known to decline with AD and thus can be used as a general indicator of the stage of the disease. The maximum score on the MMSE is 30, and lower scores are an indication of greater cognitive dysfunction. MMSE scores were grouped to match clinically identifiable levels of severity of AD: I (*early*: MMSE = 24–30); II (*mild*: MMSE = 16–23); III (*moderate*: MMSE = 9–15); IV (*moderately severe*: MMSE = 4–8); V (*severe*: MMSE = 0–3).

### The Time-based Behavioral Disturbance Questionnaire

The TBDQ<sup>5</sup> requests caregivers to report whether or not, over the previous month, the patient exhibited any of the following seven behaviors: combativeness, agitation, wandering, incoherent speech, hallucinations, confusion, and disorientation. For each behavior, appropriate definitions were provided, and respondents were asked to indicate the time periods during which the behavior took place. They were instructed to check off as many time periods as applied to each behavior. The day was divided into four time periods: morning (awakening until 12 PM); early afternoon (12 PM to 4 PM); late afternoon/evening (4 PM to 10 PM); and night (10 PM to awakening).

### TBDQ Scoring

An overall score was computed for each observation equal to the percentage of the seven behaviors across the four time periods that were checked off. This score can range from 0% (when no behaviors were reported for any time period) to 100% (when every behavior is checked off in every time period (i.e., 28 check offs)). Scores were also computed for the separate time periods as the percentage of the seven behaviors checked in each time period. These were denoted: *M* for morning, *A* for early afternoon, *E* for late afternoon/evening, and *N* for night. Finally, to provide contrast scores that offer more information about temporal patterns, two orthogonal temporal contrasts were computed as follows:

$$\text{Late day versus early day: } E - \frac{(M + A)}{2}$$

$$\text{Morning versus afternoon: } M - A$$

Thus, a particular contrast score is 0% if the behaviors are as likely to occur in the first-mentioned time period as in the contrast period (e.g., as likely in the morning as in the afternoon). The score is 100% if all of the behaviors are reported only in that time period, and -100% if none of the behaviors are reported in that time period, but are reported in all the contrast periods.

For example, in the morning–afternoon contrast, if all behaviors were reported as taking place in the morning period but no behaviors were reported as taking place in the afternoon period, the score would be 100%.

### Alzheimer's Disease Assessment Scale (ADAS)

The ADAS was designed to assess dysfunction associated with AD.<sup>7</sup> It includes both a cognitive and a noncognitive subscale. The noncognitive subscale consists of 10 items, including those that assess mood, motor activity, and psychotic symptoms. Higher scores on the ADAS indicate greater dysfunction.

### Actigraph

Rest/activity data were collected by means of an Actigraph (Ambulatory Monitoring Systems, Inc., Ardsley, NY 10502), a wrist-watch-size ambulatory motion-detecting device actually worn on the wrist. The Actigraphs were set to record motion in 30-second epochs. These data were used to measure circadian rhythmicity of rest and activity and to infer amounts of sleep and wake. The actigraph data were collected for 6-day periods. For all but four of the observations reported here, the TBDQ data were collected either simultaneously or within 1 week of the actigraph data.

### Circadian Activity Measures

Measures of circadian activity were obtained from the actigraphic recordings by using the least-squares method to compute a multiple correlation coefficient ( $R^2$ ) measure of goodness of fit to a cosine curve. In addition, the amplitude, acrophase (or peak time), and mesor (or mean activity level) were computed.

### Sleep/Wake Measures

The actigraph recordings were scored with an algorithm supplied by the manufacturer to obtain sleep measures. The computer scoring program, ACTION 1.3, requires the entry of subjects' bed times and final morning out-of-bed times. This information was taken from sleep logs completed by caregivers for each 24-hour period of actigraph recordings. Although data are collected over a 6-day period, not all data were usable due to technical faults in the mechanism. Of the data used, 72% had usable recording on 4 or 5 days, 19% on 6 or 7 days, and 9% on less than 4 days. Reported reliabilities of actigraphic-scored total sleep time compared with polysomnographic recordings have ranged from +.98 in five normal subjects<sup>8</sup> to +.84 in 25 sleep apnea subjects.<sup>9</sup>

## RESULTS

### TBDQ Raw Scores

The seven behaviors in the TBDQ were not reported with equal frequency. In order of frequency of report, they were: confusion, disorientation, agitation, incoherence, wandering, hallucinations, and combativeness. Table 1

Table 1. TBDQ Scores and Variance Component Analysis Data

Observation Samples	n	Mean TBDQ Score by Time Periods				Percentage of Variance		
		Morning	Afternoon	Evening	Night	Overall Level of Behavioral Disturbance	Consistent Temporal Patterning of Behavioral Disturbance	Stage, Subtype, Subject Inconsistencies and Observer Error
All observations including multiple observations for one subject	169	26.0	26.5	28.7	20.8	73%	2%	25%
Only the last (most recent) observation for each subject	101	30.0	28.6	33.3	23.0	72%	2%	26%
All observations including multiple observations for each subject for which there was an associated MMSE score	136	25.3	25.8	28.2	19.2	74%	2%	24%
Only the last (most recent) observation for each subject for which there was an associated MMSE score	90	25.4	24.9	27.6	19.1	77%	2%	21%

provides the sample sizes and the mean scores in each time period and the results of variance component analysis (subjects  $\times$  time period).<sup>10</sup> Because subjects might have more than one observation that may or may not have an associated MMSE score, data are presented four different ways: (1) all observations including multiple observations in one subject ( $n = 169$ ); (2) only the most recent observation for each subject ( $n = 101$ ); (3) all observations including multiple observations for each subject for which there was an associated MMSE score ( $n = 136$ ); and (4) only the most recent observation for each subject for which there was an associated MMSE score ( $n = 90$ ).

However examined, the major source of variance (73%,  $P < .001$ ) was the overall level of behavioral disturbance rather than any temporal patterning of behavioral disturbance. Although there were statistically significant differences among *M*, *A*, *E*, and *N* ( $P < .001$ ) (i.e., a consistent temporal patterning with the *E* measurement always being the highest and *N* the lowest), this consistent temporal patterning accounted for a small portion of total variance (2% overall). The remaining 25% of the total variance is determined by subtype (age of onset, or sex), stage, their interaction, or simply by random variation.

For the overall level of disturbed behavior on the TBDQ, there were significant stage effects ( $F(4, 70) = 8.88$ ,  $P < .001$ ) and sex effects ( $F(5, 70) = 3.69$ ,  $P < .001$ ), but

no significant differences between early- and late-onset cases. No significant effects were found for the contrasts. Figure 1 presents the means for the male and female AD patients by stage of illness severity.

#### Test-Retest Reliabilities and Convergent Validity

There were 14 subjects (11 male, 3 female) with two or more TBDQ observations taken in the same stage of AD. The correlation of the overall level between these observations yields an estimate of test-retest reliability

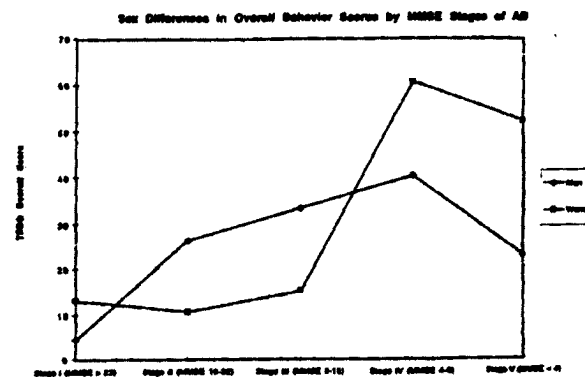


Figure 1. This graph shows the male and female stage of illness severity as indicated by the MMSE.

that was relatively high at  $r = .85$  ( $P < .01$ , one-tailed). The overall score on the TBDQ also correlated [ $r = .55$  ( $n = 85$ )  $P < .001$ , one-tailed] with the noncognitive behavioral disturbance score of the ADAS. The ADAS was completed by clinicians without the knowledge of the caregiver rating of the TBDQ. The clinicians, however, interviewed both the patient and the caregiver to obtain their ADAS ratings.

### Actigraph Measures

A total of 41 actigraphic records could be used to compute sleep/wake measures. Mean time in bed (TIB) was  $576 \pm 88$  (SD) minutes; mean total sleep time (TST) was  $435 \pm 89$  minutes; mean sleep efficiency (SE) was  $76\% \pm 13\%$ ; mean sleep onset (SO) was  $20 \pm 15$  minutes; and mean wake after sleep onset (WASO) was  $101 \pm 71$  minutes. Significant correlations were obtained between TBDQ overall score and SE [ $r = -.35$  ( $n = 41$ )  $P < .05$ ] and WASO [ $r = .43$  ( $n = 41$ )  $P < .01$ ]. Note that WASO is defined as the amount of wake time (in minutes) after sleep onset, hence a longer WASO is an indicator of bad sleep, and a shorter WASO indicates good sleep. Therefore, a positive correlation between the overall TBDQ scores and WASO indicates that higher (worse) TBDQ overall scores were associated with higher (worse) WASO scores.

A total of 48 actigraphic records were available to compute circadian-activity measures. The mean  $R^2$  was  $.65 \pm .18$  (SD), (range, .17 to .87); mean amplitude was  $42.9 \pm 11.6$ ; mean acrophase of the circadian rhythm was  $3:20$  PM  $\pm 1.1$  hour; and mean mesor was  $60.1 \pm 10.6$ . No significant correlations were obtained between any actigraphic rhythm measures and the overall score on the TBDQ.

Finally, in 38 subjects for whom both sleep and circadian-activity measures could be calculated, correlations were computed between the two sets of actigraphic measures. No significant correlations were obtained between mesor or acrophase and any sleep measures; however, amplitude correlated with TST [ $r = .44$  ( $n = 38$ )  $P < .01$ ], SE [ $r = .49$  ( $n = 38$ )  $P < .01$ ], and WASO [ $r = -.47$  ( $n = 38$ )  $P < .01$ ].

### DISCUSSION

At a descriptive level, these results confirm that caregivers' reports of disruptive behavior in AD patients at home were associated with objectively poor sleep at night, the latter assessed actigraphically. Surprisingly, caregiver reports of specifically nocturnal disruptive behavior were not correlated with these measures. There may be a number of reasons for this (see below); however, absence of statistically significant relationships between such specific features of disruptive behavior and actigraphic measures is consistent with our finding of low variance accounted for by time of day in caregiver responses to the TBDQ.

Unlike measures of simple sleep quantity, actigraphically derived assessments of circadian organization (acrophase, amplitude, mesor) were unrelated, not only to specific temporal patterns of disturbed behavior on the TBDQ, but to overall score on TBDQ as well. Inference of change (or lack thereof) in circadian organization in AD based on actigraphic data, however, must be viewed cautiously. First, it must be stressed that our patients are living in entrained conditions with exposure to a full complement of zeitgebers including, but not limited to, illumination, meals, and social influence, as well as being subjected to numerous other uncontrolled factors such as posture, exercise/activity, and even sleep. Ascertainment of components of endogenous rhythmicity under such conditions is severely compromised and may well be impossible.

Second, rest/activity represents a far-downstream behavioral output of pacemaker function in humans, the latter more typically indexed by the spontaneously occurring body temperature cycle or by the phase response curve of melatonin secretion in response to dim light. Although some investigators have interpreted actigraphic data in AD as reflecting putative changes in the circadian pacemaker itself concurrent with dementia,<sup>2</sup> masking effects on these data cannot be discounted. Ultimately, only unmasking or forced desynchrony protocols may elucidate the issue of pacemaker function in AD.

Study of more impaired populations might shed light on this issue. Work involving the use of waist-worn electronic monitors to record activity levels in 19 severely demented AD hospitalized patients found that compared to controls the AD patients had a two-fold increase in nocturnal activity.<sup>11</sup> A more recent study by this same group<sup>2</sup> examined circadian rhythms of core-body temperature and locomotor activity in 28 AD patients and 10 healthy controls. Their findings, and those of Okawa and associates,<sup>12</sup> suggest that there is a subgroup of AD patients with impaired endogenous-pacemaker function. Given these studies and our current results, future clinical trials involving disturbed behavior in AD patients should carefully consider evaluating behavior around the 24-hour day in AD patients with a wide range of severity.

Our data complement the findings of Ancoli-Israel and colleagues.<sup>1</sup> In their study, which did not employ actigraphy but incorporated 246 AD patients, longer duration of self-reported nocturnal sleep and ease of self-reported falling asleep were positively associated with severity of dementia as measured with the Mattis Dementia Rating Scale. That is, better subjective sleep was associated with greater, rather than lesser, levels of dementia. Although these relations might be predicted to some extent by known or suspected degeneration of the neural substrates for circadian rhythms in AD,<sup>13</sup> the ability of the moderately demented patients in that study (mean MMSE = 18.5) to fully comprehend and answer the questionnaire may be suspect. Longer sub-

jective sleep durations in the AD patients, for example, were correlated with caregiver reports of disruptive behavior and disorientation both at night and during the day. Because the caregivers were internally consistent (caregiver reports of aggressive behavior and night wandering were associated with higher use of sleep medication), these data suggest that caregiver reports may indeed have some validity in describing behavioral disturbance in AD, although their ability to discriminate phenomena in real time may be limited.

The TBDQ overall level of behavioral disturbance appears to have satisfactory test-retest reliability, which is encouraging because the measure is retrospective. Nonetheless, there are clear disadvantages to this method compared to direct, real-time behavioral observations as used, for example, in the study by O'Leary et al.<sup>14</sup> In that study, caregivers were asked to monitor AD patients' behavior over the 24-hour day for a period of 2 days. This type of observation increases demand on already burdened caregivers, can be done for only a limited number of days, and is difficult to do periodically in a longitudinal study or in clinical practice. By contrast, the TBDQ taxes caregivers far less, and was shown to have convergent validity with the ADAS noncognitive scale performed by a professional staff member blind to the TBDQ.

Our results suggest that the major source of variability in caregivers' reports of disruptive behaviors was the overall level of behavioral disturbance itself. A much smaller amount of the variability of the caregivers' responses was accounted for by reported temporal patterning of those behaviors. Other than presumed inability to detect such effects, several additional factors may have contributed to this pattern of results. One possibility is selection bias (i.e., patients with strong early versus late-day contrast may have been more likely to be institutionalized and thus would not have been included in our home-dwelling sample. Still another possibility is that these results could also reflect the lack of consensus in the literature about whether or not behavioral disturbance shows proclivity for time of day effects at all.<sup>15</sup> Despite numerous clinical reports and research studies of sundowning, there remains no consistent approach to measurement and little or no agreement on definition. The present results suggest that future studies of this phenomenon would do well to explore other measurement techniques, both actigraphic and observer based,<sup>16</sup> in lieu of total reliance on caregiver reports.

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