



HHS Public Access

Author manuscript

J Sleep Res. Author manuscript; available in PMC 2015 May 04.

Published in final edited form as:

J Sleep Res. 2003 December ; 12(4): 331–337.

The Sleep Disorders Inventory: an instrument for studies of sleep disturbance in persons with Alzheimer's disease

ROCHELLE E. TRACTENBERG¹, CLIFFORD M. SINGER², JEFFREY L. CUMMINGS³, and LEON J. THAL⁴

¹Department of Biomathematics and Biostatistics, Georgetown University School of Medicine, Washington, DC

²Sleep and Mood Disorders Lab, Oregon Health Sciences University, Portland, OR

³Reed Neurological Research Center, University of California, Los Angeles, Los Angeles, CA

⁴Alzheimer's Disease Cooperative Study, Department of Neurosciences, University of California, San Diego, La Jolla, CA, USA

SUMMARY

The Sleep Disorders Inventory (SDI) is an expanded version of one item of the Neuropsychiatric Inventory (NPI). It describes the frequency, severity, and caregiver burden of sleep-disturbed behaviors during a period prior to its administration. We carried out *post hoc* analyses on baseline responses to the SDI in 104 persons with Alzheimer's disease (AD) and live-in caregivers who had been recruited for a trial of melatonin in the treatment of sleep disturbance. These patient-participants averaged <7 h of sleep per night, measured by actigraph (sleep disturbance), for the 2–3-week period prior to administration of SDI. Data were from the 2 weeks prior to the baseline visit (SDI, NPI) including actigraph-derived sleep variables and 2 weeks' worth of sleep quality ratings (SQR) kept in a diary by caregivers, plus Mini-Mental State Examination and activities of daily living assessment at baseline. The prevalence of sleep disorder symptoms ranged from 34% (waking up at night thinking it is daytime) and 82% (getting up during the night). Worse SDI scores were associated with worse cognitive, functional, and behavioral status, but not with sex, age, education or duration of dementia. SDI scores were significantly worse in individuals meeting independently established criteria for a diagnosis of 'sleep disturbance' (<6 h total sleep time per night) whereas demographic variables and scores reflecting cognition and function were not significantly different across this grouping. The SDI covers a wide range of sleep behaviors and provides information independent of sleep time and SQR.

Keywords

alzheimer's disease; measurement; sleep disturbance

© 2003 European Sleep Research Society

Correspondence: Rochelle E. Tractenberg, Department of Biomathematics and Biostatistics, GCRC, Box 571457, Georgetown University School of Medicine, Washington, DC 20057-1457, USA. Tel.: 202.687.8748; fax: 202.444.4114; ret7@georgetown.edu.

INTRODUCTION

Sleep disturbances may contribute to the behavioral, functional, and cognitive status of persons with Alzheimer's disease (AD), as well as to the burden and health status of the caregiver (Pollak and Perlick, 1991; Pollak and Stokes, 1997). The Alzheimer's Disease Cooperative Study (ADCS) (Thal, 1997), an NIA-sponsored consortium of AD research centers, recently completed a large clinical study of melatonin in the treatment of sleep disturbances in persons with AD (Singer *et al.*, in press). In the present report, we describe a new instrument that assesses symptoms of sleep disturbance/disorder, the Sleep Disorders Inventory (SDI). We evaluated the responses to the SDI during the 2-week pretreatment phase of the melatonin study and describe the SDI as a novel instrument for use in assessing and quantifying sleep disturbance/disorder in AD patients.

The SDI was developed for the ADCS melatonin study and is derived from a well-known instrument, the Neuropsychiatric Inventory (NPI) (Cummings *et al.*, 1994; Mega *et al.*, 1996). The NPI is scored through a semi-structured interview by a clinician or researcher with a caregiver of the person with dementia. Night-time behaviors represent one area assessed by the NPI. The NPI can be administered and scored as a 10-item (excluding sleep and vegetative symptoms) or a 12-item instrument (including both). The SDI was created by expanding item 11 of the 12-item NPI and limiting the 'observation' period from 4 weeks to 2 weeks. According to the basic structure of the NPI, the respondent is asked a 'screening' question, a general indication of whether or not symptoms in that particular behavioral area are present. If the screening question is positive, then specific subquestions are asked. The NPI score is based on single frequency and severity ratings for the general behavioral area within the previous 4 weeks, rather than on quantitative ratings for each of the subquestions for that period.

The SDI consists of the seven subquestions from the NPI sleep disturbance item. Each of the subquestions was made into a separate question with frequency, severity, and caregiver distress rated by the caregiver with respect to the patient-participant for the 2 weeks prior to the visit. Thus, in contrast to a single rating for frequency and severity for all sleep disturbance-related behaviors, which would be incorporated into an overall NPI score, the SDI score is derived after the caregiver rates the frequency and severity of each of the seven separate sleep disturbance symptoms (see Table 3). Caregiver distress ratings are not part of the SDI total score, but distress is measured (see Table 3 and Appendix).

In addition to the SDI, participants in the melatonin study were also administered cognitive and functional instruments, the 10-item NPI, and sleep-based measures. We report here the results from the baseline (pre-randomization) period.

METHODS

We calculated the prevalence (endorsement rate) of each of the seven symptoms, as well as mean frequency, severity and caregiver impact (distress). After calculating the overall score on the SDI for each participant, we explored the relationships between the SDI and three other measures: caregiver ratings of the quality of sleep, actigraphically-measured sleep, and

behavioral symptomatology (overall NPI score). Cognitive and functional instruments (described below) were also administered to characterize the cohort at the baseline visit.

Subjects

Patient-participants were persons meeting National Institute of Neurologic and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria for probable or possible AD (McKhann *et al.*, 1984). Informed consent was obtained from all participants and their caregivers. Individuals with AD whose caregivers identified them as having disturbed sleep were screened for randomization into the melatonin study. Those meeting baseline criteria of an average of <7 h of night-time sleep during the 2–3 weeks prior to the study and/or at least two episodes of night-time awakening within the previous 2 weeks were enrolled ($n = 157$). Of these, some had mean night-time sleep time >7 h, but review of their prebaseline actigraphy revealed very low sleep efficiency (<60%) after sleep onset. Participants who had valid SDI responses at the screening visit and who resided with a caregiver ($n = 104$) were selected for this analysis, 18 of whom (17%) had mean prebaseline total sleep time (TST) >7h and were accepted by the Project Director (CS). Table 1 presents the characteristics of these AD patient-participants with respect to demographics and AD-related variables.

Instruments

Well-known and widely used instruments were used to characterize the patient-participant population. The Mini-Mental State Examination (MMSE) (Folstein *et al.*, 1975), ranging from 0 (worst) to 30 describes general cognitive functioning and is consistently used in dementia-related studies and clinical trials. The cognitive portion of the Alzheimer's Disease Assessment Scale (ADAS-Cog) (Rosen *et al.*, 1984) provides another measure of mental status, ranging from 0 to 70 (worst); both the MMSE and ADAS-Cog have good reliability and validity (Lezak, 1995). A 23-item inventory of activities of daily living (ADL) (Galasko *et al.*, 1997), with ratings by the caregiver with respect to the amount of assistance the patient requires for each activity, was administered [score ranges from 0 to 78 (worst)] to evaluate functional status. Moderate to very good short-term reliability has been reported for AD patients at all severity levels (Galasko *et al.*, 1997).

Two instruments were used to assess behavioral symptomatology, the Hamilton Depression Scale (Hamilton, 1960) and the NPI (10-item score; Cummings *et al.*, 1994). As noted earlier, for each of the 10 (or 12) behavioral areas examined in the NPI, one frequency and one severity rating is generated. The NPI total score is derived by summing the products of the frequency and severity ratings for each area [range 0–120 (worst) for the 10-item version].

Sleep-based measures

Wrist actigraphy utilizes a wristwatch-like device (Mini-Mitter Actiwatch-64; Mini-Mitter Inc., Sunriver, OR, USA) that stores information about the wearer's movements in successive minutes during 24-h periods. Periodically throughout the study, these data were downloaded to provide a continuous, computerized record of activity levels; periods where the actigraph shows no activity (time spent immobile) are interpreted as sleep. The sleep

scoring algorithm of the MiniMitter actigraph was compared with EEG-scored sleep in seven subjects with AD (not participants in the melatonin trial). In these seven subjects, actigraphy tended to overestimate sleep time by a mean of 27%, but showed excellent correlation ($r = 0.92$, $P < 0.01$) (Singer *et al.*, 2003).

Actigraphy was used to objectively estimate night-time total sleep time (NTST) as a function of time spent immobile between 20.00 and 08.00 hours averaged over 2–3 weeks prior to the baseline visit. Similarly, average daytime total sleep time (DTST) was estimated from the immobility data over this period for the 08.00–20.00 hours epoch. We estimated 24-h TST as the sum of DTST and NTST values averaged over the prebaseline period, and the average of the daily ratios of DTST/NTST reflected the ratio of time spent asleep during the day to that during the night. The actigraphy data files for each patient-participant reflected the number of minutes of mobility (time awake) between sleep onset (i.e. the onset of immobility after bedtime) and final awakening [i.e. the (last) onset of mobility immediately before the end of the night-time epoch or the end of the epoch], which was calculated for each night in the prebaseline period and averaged for an estimate of time awake after sleep onset (WASO). Similarly, the ratio of NTST to total time between sleep onset and final awakening expressed as a percentage was calculated for each night in the prebaseline period and averaged for an estimate of sleep efficiency (SE).

In addition to the actigraph-based variables, caregivers gave a daily sleep quality rating (SQR) in their sleep diary. For each morning during the prebaseline period, caregivers rated the patient-participant's sleep on a five-point scale (0 = very poor night with little or no sleep; 1 = difficult night with several awakenings or a long period without sleep; 2 = fair night with only few, brief (<30 min) awakenings; 4 = good night with only one, brief (<30 min) awakening; 5 = outstanding night with no awakenings). These daily ratings were averaged for an SQR for the prebaseline period.

The SDI was administered at the baseline visit, where caregivers were asked to provide ratings for the frequency, severity and their distress with respect to the seven symptoms in the previous 2-week period. The number (of seven) items endorsed (i.e. rated as having occurred at least once per week) was recorded, and the SDI score was derived as the product of the average of the frequency ratings and the average of the severity ratings [range: 0–12 (worst)]. The SDI is included in the Appendix.

Statistical methods

Several analyses were carried out to assess the relationship between SDI score and both sleep- and non-sleep variables. First, to evaluate convergent validity between the SDI and other sleep measures, correlations were calculated between the SDI scores and all sleep-related variables: SQR, NTST, DTST, DTST/NTST, sleep efficiency, WASO, and 24 h TST (NTST + DTST). Secondly, to assess the impact of non-sleep variables on SDI scores, correlations were calculated between the SDI scores and all non-sleep related variables: age, AD duration, education, MMSE, ADAS, ADL, Hamilton and NPI. Finally, to evaluate the performance of the SDI in a clinical or applied sense, mean frequency, severity and caregiver distress ratings were compared across patient gender. These values as well as number of SDI items endorsed, and SDI score were compared by independent samples *t*-

tests in study participants who met the definition of sleep disturbance ‘less than 6 h NTST’ (Yesavage *et al.*, 2003) with those with 6 h or more NTST (measured by actigraphy averaged over the prebaseline period).

All analyses were performed using SPSS version 11.0 (2000; SPSS Inc., Chicago, IL, USA). As the population was recruited based on disturbed sleep, normality of the distributions of values for sleep variables was unlikely. Therefore, means and standard deviations for scores were calculated, along with modal values, for ratings of SDI symptoms. Also, nonparametric correlations (Spearman’s rho) and *t*-tests were performed. *P*-values for the *t*-tests were adjusted according to Holm (1979) and adjusted *P* < 0.05 were considered significant.

RESULTS

Cohort characteristics

Over a 2-year recruitment period involving 36 research centers, 244 persons were screened and 157 participants (64%) were ultimately enrolled in the melatonin study (Singer *et al.*, 2003). The 104 patient-participants described here had a mean age of 75.5 ± 8.6 years, reported an average of 12.6 ± 3.8 years of education and were diagnosed with AD an average of 4.6 ± 3.0 years prior to enrollment (see Table 1). Roughly half (49%) were female and on average, participants were moderately demented (mean MMSE 15.5 ± 8.4), although the range of severity was wide [MMSE scores from 0 to 30 and ADAS scores from 8 to 69 (although an MMSE ≥ 26 was an inclusion criterion, a few exceptions were made if the site principal investigator [all experienced, NIA-funded dementia researchers] felt that the clinical diagnosis could be made on the basis of history and other testing, such as the Clinical Dementia Rating scale)].

Table 2 presents the sleep-related measures excluding the SDI. Recruitment to the melatonin study was primarily focused on patient-participants who experienced an average NTST of <7 h, and actigraph-based estimates of NTST show that on average, the cohort described here had an average of 6 h (364.4 min) during the prebaseline period. Individuals who had more than 7 h of NTST during the prebaseline period were admitted to the study if their sleep was particularly fragmented. This was the case for 18 participants with valid NTST values in this cohort (17%).

On average, SQR for the 2-week observation period indicated that the typical participant experienced ‘fair’ sleep at night, with few, brief awakenings (mean 3.1 ± 0.7).

SDI characteristics

Two values were calculated based on the SDI-item responses. The SDI score (average of seven frequency ratings \times average of seven severity ratings) was 3.6 (SD: 2.2), with scores ranging from 0.6 to 10.3. On average, four of the seven items were rated as occurring at least once per week (SD: 1.6). The average frequency rating over the seven items was 1.9 (SD: 0.8), corresponding to a rating of ‘frequently’ (i.e. more than ‘once per week’ but less than ‘daily’). The average severity rating was 1.7 (SD: 0.5), roughly corresponding to a rating of ‘moderate’. The average level of caregiver distress was 2.2 (SD: 1.1), corresponding to ‘mild’ distress. Table 3 presents the item-level descriptive statistics for the SDI symptoms.

The modal frequency for five of the seven items on the SDI was zero, namely, the most frequently observed ratings indicated that difficulty in falling asleep (item 1), inappropriate night-time activities (item 3), waking up and thinking it to be daytime (item 5), awaking earlier than previously (too early) (item 6) and excessive sleeping during the day (item 7) did not occur in the 2 weeks prior to the baseline visit in this cohort. The two other items (getting up at night, item 2; awakening caregiver, item 4) had modal frequency ratings of 4, corresponding to occurring every night.

For SDI symptoms that the caregiver rated as having occurred at least ‘less than once per week’ (i.e. not those rated as ‘not present in last 2 weeks’), the modal severity rating was ‘mild – not particularly disruptive’ only for two items (difficulty falling asleep and sleeping during the day). For the five other SDI symptoms, the modal severity rating was ‘moderate’, indicating that these behaviors were disruptive to both the patient and the caregiver. The only symptom that was not rated ‘moderately’ emotionally distressing by the majority of caregivers in this sample was excessive sleeping during the day.

SDI and sleep variables

The SDI score (product of the average of frequency ratings for seven items and the average of severity ratings for seven items) was associated with every sleep variable except DTST and 24 h TST. SDI scores were negatively related to the mean SQR to a significant extent ($\rho = -0.277$, $P = 0.006$); significant negative association was also observed with NTST ($\rho = -0.244$, $P = 0.014$) and sleep efficiency ($\rho = -0.283$, $P = 0.004$). Positive and significant association was observed between SDI and WASO ($\rho = 0.243$, $P = 0.014$) and the ratio of DTST/NTST ($\rho = 0.215$, $P = 0.030$). The correlations between the sleep variables appear in Table 4.

The number of sleep disturbance symptoms endorsed (rated at least once per week) was not associated with SQR, WASO or 24 h TST, but was associated in the same direction and to similar extents with the other variables as the SDI score itself (SDI score and number of symptoms endorsed had a strong, positive correlation).

The average SQR over the prebaseline period was significantly associated with every sleep variable except 24 h TST. Associations between this sleep diary value with SE ($\rho = 0.490$, $P < 0.01$) and WASO ($\rho = -0.412$, $P < 0.01$) were the strongest.

SDI and non-sleep variables

Worse SDI scores were significantly associated with worse MMSE, ADAS, ADL, Hamilton and NPI scores (all $P < 0.05$). Correlations are presented in Table 4.

No association between patient gender and the components of the SDI score was observed, that is, frequency, severity, distress, number of symptoms endorsed and SDI scores were not different for men and women (all $P > 0.12$). SQR were not associated to a significant degree with any non-sleep variable (all $P > 0.06$). Neither variable was significantly associated with age (both $P > 0.15$), education (both $P > 0.18$) or duration of AD (both $P > 0.60$).

Clinical/practical utility of SDI

Finally, this cohort was divided into two groups according to a 6 h NTST criterion (i.e. <6 h NTST representing disturbance and ≥6 h representing no disturbance) recently proposed as a marker of sleep disturbance in persons with AD (Yesavage, *et al.*, 2003). Table 5 contains the means and standard deviations of SDI, SQR and non-sleep scores/values for the two groups.

Individuals with an average of at least 6 h of NTST by actigraphy during the prebaseline period (i.e. patients not meeting this sleep disturbance criterion) reported significantly lower severity and caregiver distress related to the seven SDI items; they had significantly lower SDI scores at baseline (all adjusted $P < 0.05$) and endorsed fewer items (adjusted $P < 0.09$) than did individuals with <6 h of NTST. SQR were very similar for the two groups (roughly equivalent to 'fair' for both; adjusted $P > 0.05$). The groups were not different in terms of gender breakdown, age, years since diagnosis of AD, years of education, MMSE, ADAS, ADL, NPI or Hamilton scores (all adjusted $P > 0.05$).

DISCUSSION AND CONCLUSIONS

The symptoms of sleep disturbance contained in the SDI were endorsed between 34% (waking up at night thinking it to be daytime) and 82% (getting up during the night) of live-in caregivers for this AD patient cohort ($n = 104$). Night-time wandering and awakening the caregiver were the two items causing the highest level of caregiver distress, whereas daytime sleeping caused the least; these results are similar to those reported by McCurry *et al.* (1999) in an independent, population-based sample of community-dwelling persons with AD who were not specifically sleep disturbed.

Total SDI score was not associated with patient sex, education or dementia duration, but was cross-sectionally associated with worse dementia in this cohort with severity ranging from mild to severe; these results echo those reviewed and reported by Moe *et al.* (1995) based on REM, not actigraphic, objective sleep data. In a recent study of nondemented adult insomniacs and healthy matched adult controls, Voderholzer *et al.* (2003) reported that neither objective (polysomnography-based) nor subjective reports of sleep disturbance was associated with respondent sex. Studies of sleep and circadian rhythms in older adults and those with dementia have only inconsistently shown gender differences in daytime sleepiness, insomnia, and circadian phase (Bliwise, 1999). These earlier findings support the validity of our results with the SDI and actigraphy.

The SDI scores correlated with every actigraph-derived sleep measure except for 24 h TST and DTST. This again indicates that in this cohort of subjects, caregivers were distressed mainly by night-time behaviors, and not daytime sleeping. This would likely be true of most caregivers, although the sample of caregivers in this study were a select group in that they had enrolled in a clinical trial for melatonin treatment of night-time sleep disturbance. Excessive daytime sleeping was one of the three most frequently endorsed behaviors and caused the least distress (see Table 3). It is possible that caregivers were not aware that maintaining proper sleep hygiene (e.g. not napping during the day; Neubauer, 1999) might decrease sleep disturbance; while the typical caregiver might value a respite provided by

daytime sleepiness, it is possible that they are not aware that they may be, in effect, trading their own night-time sleep for this daytime break.

The SDI also differentiated individuals with <6 h of NTST and those with at least 6 h of NTST in terms of SDI score, mean severity and caregiver distress associated with each of the seven component items. These values were significantly worse for individuals averaging <6 h NTST. After adjustments for multiple comparisons, average frequency ratings did not differ between individuals grouped according to the 6-h criterion, and number of symptoms endorsed was marginally non-significant (adjusted $P = 0.09$). Average frequency and number of symptoms endorsed were both worse for the individuals with <6 h NTST, and the failure of these differences to reach significance may be the result of the fact that all patient-participants were known to have disturbed sleep. Future studies of the validity of the SDI with individuals without sleep disturbance are needed.

In these persons with disturbed sleep and AD, the SDI was found to be orthogonal to other sleep-related measures, explaining <25% of the variance in any one measure. These results suggest that there is some degree of commonality for SDI and these sleep-related measures, but not enough to characterize the SDI as overlapping with these measures. That is, the SDI contributes unique information about sleep disturbance by incorporating the caregiver's perspectives on severity and distress. The SDI scores indicate that a definition of sleep disturbance in AD patients that relies only on a threshold of TST will not fully reflect the caregiver's perspective captured by the SDI. We believe that the SDI score reflects salient symptomatology with respect to sleep disturbance. However, because of the scoring algorithm, intraclass correlation coefficients are not interpreted in a straightforward manner. In future studies we plan to evaluate the internal structure of the inventory.

The SDI is a simple and short instrument that can be administered once to characterize the period before an evaluation (2 weeks in this example), and can be administered at a screening or first evaluation visit. Conversely, a sleep diary such as that generating the SQR used in this study must be filled out each day during the same 2-week period before the screening visit, adding an additional visit (and extra 2 weeks) to a study protocol or to the evaluation of a patient's sleep disturbance.

In conclusion, we have demonstrated the validity of using the sleep questions of the NPI as an independent instrument (i.e. the SDI) in sleep research requiring a caregiver's report of sleep symptoms by showing good correlation, but not redundancy, with quantitative sleep measurements, including the 6 h NTST criterion. In terms of the impact on caregivers of sleep disturbance in co-residing persons with AD, we have also shown that night-time awakening, and not daytime sleeping, causes considerable caregiver distress. The SDI might be improved if it included items that refer to the caregiver's sleep, to provide a general idea of the extent to which their sleep was disrupted during the period covered by the SDI questions. We believe that the SDI fills a need for practical and experimental/clinical trial sleep instrument in the AD population.

Acknowledgments

The study was supported by Grant AG 10483 from the National Institute on Aging.

References

- Bliwise, D. Sleep disorders in aging and dementia. In: Turk, FW.; Zee, PC., editors. Regulation of Sleep and Circadian Rhythms. Marcel Decker, Inc; New York, NY: 1999. p. 498-499.
- Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. *Neurology*. 1994; 44:2308–2314. [PubMed: 7991117]
- Folstein MF, Folstein SE, McHugh PR. 'Mini-Mental State': a practical method for grading the cognitive state of patients for the clinician. *J Psychiatric Research*. 1974; 12:189–198.
- Galasko D, Bennet D, Sano M, Ernesto C, Thomas R, Grundman M, Ferris S. and the Alzheimer's Disease Cooperative Study. An inventory to assess activities of daily living for clinical trials in Alzheimer's disease. *Alz Dis Assoc Disord*. 1997; 11(Suppl 2):S33–S39.
- Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960; 23:56–62. [PubMed: 14399272]
- Holm S. A simple sequentially rejective multiple test procedure. *Scan J Stat*. 1979; 16:65–70.
- Lezak, MD. *Neuropsychological Assessment*. 3. Oxford Press; New York, NY: 1995.
- McCurry SM, Logsdon RG, Teri L, Gibbons LE, Kukull WA, Bowen JD, McCormick WC, Larson EB. Characteristics of sleep disturbance in community-dwelling Alzheimer's disease patients. *J Geriatr Psychiatry Neurol*. 1999; 12:53–59. [PubMed: 10483925]
- McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA work group under the auspices of the Department of Health and Human Services Task Force on Alzheimer's disease. *Neurology*. 1984; 34:939–944. [PubMed: 6610841]
- Mega MS, Cummings JL, Fiorello T, Gornbein J. The spectrum of behavioral changes in Alzheimer's disease. *Neurology*. 1996; 46:130–135. [PubMed: 8559361]
- Moe KE, Vitiello MV, Larsen LH, Prinz PN. Symposium: cognitive processes and sleep disturbances: sleep/wake patterns in Alzheimer's disease: relationships with cognition and function. *J Sleep Res*. 1995; 4:15–20. [PubMed: 10607136]
- Neubauer DN. Sleep problems in the elderly. *Am Fam Physician*. 1999; 59:2551–2560. [PubMed: 10323361]
- Pollack CP, Perlick D. Sleep problems and institutionalization of the elderly. *J Geriatr Psychiatry Neurol*. 1991; 4:204–210. [PubMed: 1789908]
- Pollak CP, Stokes PE. Circadian rest-activity rhythms in demented and nondemented older community residents and their caregivers. *J Am Geriatr Soc*. 1997; 45:446–452. [PubMed: 9100713]
- Rosen WG, Mohs RC, Davis KL. A new rating scale for Alzheimer's disease. *Am J Psychiatry*. 1984; 141:1356–1364. [PubMed: 6496779]
- Singer C, Tractenberg RE, Kaye J, Gamst A, Grundman M, Thomas RG, Thal LJ. A multicenter clinical trial of melatonin for sleep disturbance in Alzheimer's disease. *Sleep*. 2003; 26:893–901. [PubMed: 14655926]
- Thal LJ. Development of the Alzheimer's Disease Cooperative Study. *Int J Geriatr Psychopharmacol*. 1997; 1:6–9.
- Voderholzer U, Al-Shajlawi A, Weske G, Feige B, Riemann D. Are there gender differences in objective and subjective sleep measures? A study of insomniacs and healthy controls. *Depression and Anxiety*. 2003; 17:162–172. [PubMed: 12768650]
- Yesavage JA, Friedman L, Ancoli-Israel S, Bliwise D, Singer C, Vitiello MV, Monjan AA, Lebowitz B. Development of diagnostic criteria for defining sleep disturbance in Alzheimer's disease. *J Geriatr Psychiatry Neurol*. 2003; 16:131–139. [PubMed: 12967054]

APPENDIX: SLEEP DISORDERS INVENTORY

Directions: Ask the subject's principal caregiver to indicate whether any of the subject behaviors listed below occurred during the previous 2 weeks. If so, use the following scales to rate the frequency, severity and amount of distress each causes the caregiver.

Symptom

- 1 Difficulty falling asleep
 - 2 Getting up during the night (do not count if the subject gets up once or twice per night to go to the bathroom and quickly falls back to sleep)
 - 3 Wandering, pacing or getting involved in inappropriate activities at night
 - 4 Awakening you during the night
 - 5 Awakening at night, dressing, and planning to go out, thinking that it is morning and time to start the day
 - 6 Awakening too early in the morning (earlier than is his/her habit)
 - 7 Sleeping excessively during the day
 - 8 Other night-time behaviors that bother you
-

Frequency

- 0: Not present in the last 2 weeks
- 1: Less than once per week
- 2: One to two times per week
- 3: Several times per week but less than every day
- 4: Once or more per day (every night)

Severity

- 0: Not present
- 1: Mild: night-time behaviors occur but are not particularly disruptive
- 2: Moderate: night-time behaviors occur and disturb the patient and the sleep of the caregiver; more than one type of night-time behavior may be present
- 3: Marked: night-time behaviors occur; several types of night-time behavior may be present; the patient is very distressed during the night and the caregiver's sleep is markedly disturbed

Caregiver Distress: How emotionally distressing do you find this behavior?

- 0: Not at all
- 1: Minimally
- 2: Mildly
- 3: Moderately
- 4: Severely
- 5: Very severely/extremely

Table 1

Descriptives for 104 study participants at baseline

<i>Score/value</i>	<i>Mean ± SD</i>	<i>Minimum–maximum (n)</i>
Age (years)	75.5 ± 8.6	47–92 (104)
Gender (% female)	49%	(104)
Education (years)	12.6 ± 3.8	0–20 (104)
Duration of Alzheimer’s disease (years)	4.6 ± 3.0	0–20 (104)
Mini-Mental State Examination	15.5 ± 8.4	0–30 (102)
Alzheimer’s Disease Assessment Scale	34.4 ± 18.7	8–69 (98)
Activities of daily living	40.7 ± 22.7	4–77 (104)
Hamilton Depression Scale	7.7 ± 3.5	0–16 (104)
Neuropsychiatric Inventory (10-item)	19.7 ± 16.7	0–68 (104)

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 2

Sleep related variables for 104 study participants averaged over prebaseline period

<i>Score/value</i>	<i>Mean ± SD</i>	<i>Minimum–maximum (n)</i>
Sleep quality rating	3.1 ± 0.7	1.5–4.9 (99)
Night-time TST*	364.4 ± 69.4	177.3–519.6 (102)
Daytime TST*	147.6 ± 95.0	14.2–509.3 (102)
24 h TST*	512.0 ± 127.4	257.0–949.6 (102)
DTST/NTST	0.5 ± 0.5	0.04–4.7 (102)
Wake after sleep onset*	156.7 ± 53.7	41.0–328.0 (102)
Sleep efficiency	0.7 ± 0.1	0.41–0.91 (102)
Number of actigraph observations	13.4 ± 5.1	1–21 (102) [†]

TST: total sleep time; Daytime: 08.00–20.00 hours; night-time: 20.00–08.00 hours.

* Given in minutes.

[†]Two individuals had zero actigraph observations during prebaseline period.

Table 3

Sleep Disorders Inventory: item level descriptive statistics

Symptom*	Frequency (0-4)	Severity (0-3)	Distress [†] (0-5)	Endorsement [‡]	Mod/Marked severity [§]	Mod/extreme distress [¶]
Difficulty falling asleep	1.6 ± 1.7; 0	1.8 ± 0.8; 1	2.0 ± 1.5; 3	47.2%	54.5%	42.6%
Getting up during the night (do not count if the subject gets up once or twice per night to go to the bathroom and quickly falls back to sleep)	2.9 ± 1.04; 4	1.9 ± 0.7; 2	2.3 ± 1.4; 3	82.1	71.7	47.3
Wandering, pacing or getting involved in inappropriate activities at night	1.9 ± 1.7; 0	1.9 ± 0.7; 2	2.7 ± 1.4; 3	57.1	69.8	55.6
Awakening you during the night	2.4 ± 1.6; 4	1.9 ± 0.7; 2	2.6 ± 1.3; 3	67.9	72.0	54.9
Awakening at night, dressing, and planning to go out, thinking that it is morning and time to start the day	1.2 ± 1.5; 0	1.8 ± 0.7; 2	2.4 ± 1.4; 3	34.3	64.6	58.4
Awakening too early in the morning (earlier than is his/her habit)	1.7 ± 1.6; 0	1.8 ± 0.7; 2	2.2 ± 1.6; 3	51.4	65.0	51.7
Sleeping excessively during the day	2.0 ± 1.7; 0	1.5 ± 0.7; 1	1.3 ± 1.4; 0	58.5	40.3	23.9

Values are expressed as mean ± SD; mode, or percent.

* These symptoms are from 'The Neuropsychiatric Inventory: Comprehensive assessment of psychopathology in dementia', by J. L. Cummings, M. Mega, K Gray, et al., *Neurology* 1994; 44, p. 2314. Copyright 1994 by J. L. Cummings. Adapted with permission.

[†] Caregiver's distress rating;

[‡] proportion of group rating symptom as occurring at least once per week;

[§] proportion of group reporting moderate or marked severity;

[¶] proportion of group expressing moderate to extreme distress.

Frequency ratings (relative to the past 2 weeks): 0 = not present; 1 = less than once per week; 2 = 1-2 times per week; 3 = several times per day but less than every day; 4 = once or more per day (every night).

Severity ratings: 0 = not present; 1 = mild; 2 = moderate; 3 = marked (see Appendix for more detail). Caregiver distress ratings (how emotionally distressing is the behaviour?): 0 = not at all; 1 = minimally; 2 = mildly; 3 = moderately; 4 = severely; 5 = very severely/extremely.

Table 4

Nonparametric correlations: SDI, number of SDI symptoms (0–7), and SQR with sleep and non-sleep variables

	<i>SDI</i>	<i>No. of SDI SX</i>	<i>SQR</i>
Sleep variables			
SDI	1.000	0.838*	-0.277*
SQR	-0.277*	-0.184	1.000
NTST	-0.244 [†]	-0.227 [†]	0.316*
DTST	0.114	0.165	-0.282*
SE	-0.283*	-0.217 [†]	0.490*
WASO	0.243 [†]	0.175	-0.412*
DTST/NTST	0.215 [†]	0.244 [†]	-0.387*
24HTST	-0.084	-0.045	-0.007
Non-sleep variables			
MMSE	-0.406*	-	0.192
ADAS	0.459*	-	-0.161
Hamilton	0.227 [†]	-	-0.044
NPI	0.341*	-	-0.074
ADL	-0.451*	-	0.121

* $P < 0.05$;

[†] $P < 0.01$.

SQR, sleep quality rating; SDI, Sleep Disorders Inventory; #SDI SX, number of SDI symptoms occurring at least once per week. NTST, night-time total sleep time; DTST, daytime total sleep time; SE: sleep efficiency; WASO, time awake after sleep onset; 24 h TST: DTST + NTST; MMSE, Mini-Mental State Examination; ADAS, Alzheimer's Disease Assessment Scale; Hamilton, Hamilton Depression Scale; NPI, Neuropsychiatric Inventory (10-item score); ADL, activities of daily living.

Table 5Comparison of SDI and non-sleep variables for subjects with <6 h or 6 NTST, and unadjusted *P*-value

	<i>Less than 6 h TST (n = 44)</i>	<i>6 h+ TST (n = 58)</i>	<i>Unadjusted P-value</i>
Age	75.2 (8.1)	75.6 (9.1)	0.791
Gender (% female)	43.2%	51.7%	0.392
Education (years)	12.3 (4.0)	13.0 (3.8)	0.434
Duration of AD (years)	5.3 (3.5)	4.2 (2.4)	0.060
MMSE	14.6 (9.2)	16.6 (7.6)	0.232
ADAS	38.3 (20.9)	31.0 (16.1)	0.066
ADL	39.1 (22.2)	42.9 (22.7)	0.398
Hamilton	7.7 (3.6)	7.7 (3.5)	0.908
NPI	25.0 (18.1)	15.8 (15.1)	0.006
SDI score (avg. frequency × avg. severity)	4.3 (2.3)	3.0 (1.9)	0.002*
Average frequency rating	2.2 (.8)	1.8 (.7)	0.009
Average severity rating	1.9 (.5)	1.6 (.5)	0.003*
Average CG distress rating	2.5 (1.2)	1.8 (1.0)	0.002*
Number of SDI symptoms present	4.3 (1.6)	3.6 (1.6)	0.007
Sleep quality rating (average)	2.9 (0.7)	3.2 (0.7)	0.043

Values are expressed as mean (SD).

* Holm-adjusted *P*-value < 0.05; *n* = 102 as two subjects had no actigraphy.

TST, total sleep time; AD, Alzheimer's Disease; MMSE, Mini-Mental State Examination; ADAS, Alzheimer's Disease Assessment Scale; ADL, activities of daily living; NPI, Neuropsychiatric Inventory; SDI, Sleep Disorders Inventory; Avg, the average over the seven items for an individual; CG, caregiver.