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Rest-Activity and Behavioral Disruption in a Patient with Frontotemporal Dementia

J. Merrilees⁽¹⁾, E. Hubbard⁽²⁾, J. Mastick⁽²⁾, B.L. Miller⁽¹⁾, and G.A. Dowling⁽²⁾

⁽¹⁾ University of California, San Francisco Memory and Aging Center

⁽²⁾ University of California, San Francisco School of Nursing

Abstract

The neurological deterioration in dementia is associated with disturbances in circadian rhythms and rest-activity patterns. These disruptions have been documented in Alzheimer's disease (AD) and dementia with Lewy bodies but little is known about rest-activity patterns in patients with frontotemporal dementia (FTD). We report longitudinal (2 year) actigraphy results for a patient who met diagnostic criteria for FTD and his family caregiver. The subject and his family caregiver wore Actiwatches continuously for 2-weeks at 1-year intervals. The findings suggest that with disease progression there is worsening in multiple areas of rest-activity measures for the patient and a negative impact on sleep quality for the family caregiver.

Keywords

Frontotemporal dementia; actigraphy; circadian rhythm; rest-activity; sleep-wake

Introduction

Dementia is a progressive condition leading to disability and death and is associated with significant economic and societal burden (Langa et al., 2001; Moore, Zhu, & Clipp, 2001). Frontotemporal lobar degeneration (FTLD) accounts for 12-16% of all primary degenerative dementias (Brun, 1987; Neary et al., 1998) and is the most common cause of dementia in people under the age of 60 (Knopman, Petersen, Edland, Cha, & Rocca, 2004; Ratnavalli, Brayne, Dawson, & Hodges, 2002). FTLD typically occurs in the 5th and 6th decade with symptoms resulting from deterioration of the frontal and/or anterior temporal lobes of the brain. Three distinctive clinical subtypes of FTLD have been described. There are two subtypes associated with progressive changes in language, while the other and most common subtype, frontotemporal (FTD) is characterized by disinhibition, aberrant motor behaviors (e.g., restlessness, and/or compulsive or stereotypic rituals), loss of sympathy and empathy for others, apathy, and hyperorality or appetite disturbance (Bathgate, Snowden, Varma, Blackshaw, & Neary, 2001; Diehl & Kurz, 2002; Ikeda, Brown, Holland, Fukuhara, & Hodges, 2002; Lindau et al., 2000; Liu et al., 2004; Marczyński, Davidson, & Kertesz, 2004; Rosen et al., 2005).

Rest-activity rhythms capture patterns of movement and in most individuals; there are higher levels of purposeful movement during the daytime with lower levels of movement during the night. Variables used to describe rest-activity characteristics include circadian rhythm parameters, sleep and wake variables, sleep architecture parameters, and behavioral symptoms. The neurological deterioration in dementia contributes to disturbances in rest-activity rhythm. These changes have been documented in AD (Witting, Kwa, Eikelenboom, Mirmiran, & Swaab, 1990; Yesavage et al., 1998) and include behavioral symptoms such as

nighttime wandering and agitation (Ancoli-Israel, Klauber, Gillin, Campbell, & Hofstetter, 1994; Volicer, Harper, Manning, Goldstein, & Satlin, 2001) and decreased daytime activity (Pollak & Stokes, 1997). Dementia with Lewy bodies is also associated with rest-activity disruptions (Grace, Walker, & McKeith, 2000; Harper et al., 2004) that include fluctuations in alertness and abnormal motor symptoms during sleep (Boeve et al., 1998).

In this study we evaluated the longitudinal changes in movement in a patient with FTD, while simultaneously measuring the effects of this movement on the patient's partner.

Case report

WS was 58 years old when he presented to the clinic with his partner (female age 53) of many years for evaluation of behavioral and cognitive changes. His symptoms began approximately 3-4 years earlier when he began dressing more casually and put off showering for days at a time. Socially inappropriate behaviors included increased temper, emotional outbursts, rude comments, and personal discussions with strangers. WS developed several compulsive habits including watching television all day, checking his temperature every morning, and making lists of actors from particular television programs. He began purchasing videos and other merchandise, spending \$8,000 to \$10,000 per month on video purchases alone. Symptoms of apathy also developed concurrently. WS stopped engaging in many activities that he had previously greatly enjoyed, such as exercise, photography, computer programming, and withdrew from friends. Cognitive changes included increased difficulty with executive function and problems with organization and planning. He neglected to pack for vacations until the last minute and would then put only a few items in a suitcase. At the time of his first evaluation, WS was able to drive, handle finances, and shop and cook for himself independently. He no longer worked, expressed no desire to look for a job, and was increasingly indifferent to hygiene and appearance. He developed cravings for sweets and carbohydrates. Neuropsychological testing revealed minimal cognitive impairment with predominant deficits in the areas of executive function. Visual memory was intact, but verbal memory was slightly below average. Performance on visual spatial tasks was relatively preserved. His neurological examination was unremarkable, but he revealed a significant degree of depressive symptomatology. Behavioral symptoms included apathy, disinhibition, irritability, aberrant motor behaviors, and overeating. By history, sleep was normal. Current medications included daily doses of Reminyl 8 mg, Sertraline 200 mg, Tamsulosin 0.4 mg and herbal supplements. The MRI revealed generalized atrophy, with the most significant atrophy in the right frontal lobe. These findings were judged to be consistent with a neurodegenerative process, and WS was given the diagnosis of FTD.

Year 2

WS's apathy had increased and he spent most of his days watching television. His compulsive purchasing had diminished. He was relatively calmer and had few emotional outbursts, but now refused to engage in any physical activity and rarely left the house. Social inappropriateness continued and he appeared more childish in social situations. His craving for sugar and carbohydrates remained the same. Cognitively, he showed increased forgetfulness and on one episode left the coffee pot on the stove. Neuropsychological testing revealed mild cognitive impairment and he continued to demonstrate executive dysfunction and impulsivity. His visual spatial and language skills remained relatively spared. Behavioral symptoms included profound apathy and repetitive habits (burped and cleared throat constantly). He no longer endorsed depression. He stayed in bed most of the day, arising to use the bathroom, and occasionally going to see a movie. During the examination, he was less engaged in conversation and demonstrated little insight about his functional

decline. Current medications included daily doses of Sertraline 200 mg and Tamsulosin 0.4 mg. His weight was 277 pounds.

Year 3

WS now exhibited very poor memory, poor attention, and no insight into his condition. His partner described conversations that were “bizarre” and felt there were times in which he did not recognize her. He spent the majority of his time in bed with the television on, but was unable to stay focused on programs for long. He wrote compulsively on the margins of books. He now awakened his partner during the night to inform her he was going to the bathroom. During the examination he perseverated on movies and conversations were tangential. He complained of feeling tired and sighed frequently. The preference for sugar and carbohydrates persisted. WS wore clothing that was rumpled and stained. Cognitive skills declined slightly. Behavioral symptoms included frequent daytime napping, apathy, and repetitive habits. At this visit, WS and his partner consented to participate in the actigraphy study. His only medication was Sertraline 200 mg daily. His weight was 302 pounds, an increase of 25 pounds in one year.

Year 4

WS exhibited profound apathy and complained of profound fatigue. He rarely left bed, spending his days with the television on, seemingly indifferent to the programs. He was unable to complete much of the cognitive testing battery. Behavioral symptoms were apathy and sleep complaints (difficulty falling asleep and multiple nighttime awakenings). He continued to wake his partner to inform her he was going to the bathroom and sometimes awakened her just to pick up her hand. Medications included Sertraline 200 mg daily, and evening doses of Levothyroxine, Tamsulosin, Tylenol PM, and Benadryl (doses unavailable). His weight was 293 pounds.

Two months prior to the patient's death, he was moved to a long-term care facility. Postmortem analysis of brain tissue showed numerous tau positive neuronal and glial inclusions including Pick bodies and ballooned neurons in the neocortex and the hippocampus, dentate gyrus, and amygdala. An unexpected postmortem finding was evidence of chronic lymphocytic leukemia (CLL), pulmonary thromboemboli, and remote cardiovascular infarcts.

Methods

Subjects and Procedures

The patient and his family caregiver were recruited from an NIH-funded Program Project Grant (PPG) exploring FTLT entitled “Genes, Images and Emotions.” Participants undergo comprehensive annual evaluations. WS and his caregiver participated in the actigraphy protocol at the 3rd and 4th year of their enrollment in the PPG. They consented to simultaneously wear Actiwatchs to record their activity. They were instructed to affix the Actiwatchs to their nondominant wrist and to wear them continuously for 14 consecutive days. The subjects were instructed to follow their normal day and night routine.

Apparatus

Rest-activity was recorded in one-minute epochs with an Actiwatch (AW-64, Mini Mitter Co. Inc., Bend, OR, USA). Actiwatchs are compact, wrist-worn, battery-operated activity monitors whose physical characteristics are similar to a small wristwatch. Actiwatchs use a sensor known as an “accelerometer” to monitor the occurrence, degree and speed of motion and produce a signal whose magnitude and duration depend on the movement-induced accelerations. The signal is amplified and digitized by the on-board circuit. This information

is stored in memory on board the device as activity counts in one-minute epochs. Actigraphy is an accepted method for studying the rest-activity rhythm in patients with dementia (Ancoli-Israel et al., 2003; Littner et al., 2003). In addition, actigraphy has been used to quantify day and night behavioral interactions between community dwelling people with dementia and their caregivers (Brown, Smolensky, D'Alonzo, & Redman, 1990; Pollak, Stokes, & Wagner, 1997), thus providing a way to monitor rest and activity in the home versus in an artificial setting such as a laboratory.

Measures

The caregiver recorded their daily sleep and wake time on sleep logs as well as any time the watches were not in place. She completed the Pittsburgh Sleep Quality Index (PSQI) for herself and the Epworth Sleepiness Scale (ESS) on the patient. The PSQI was developed for use in clinical practice and research and is composed of 19 self-rated items (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989). Domains covered by the PSQI include subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medications, and daytime dysfunction. The format is 15 multiple-choice questions and 4 write-in items. Seven component scores corresponding to the domains are generated; each component score ranges from 0 (no difficulty) to 3 (severe difficulty). The component scores are added together for a global score (range of 0-21). A global score > 5 is suggestive of poor sleep quality indicating the respondent (in this project, the family caregiver) is experiencing severe difficulties in at least 2 areas or moderate trouble in more than three areas. The ESS rates the likelihood of dozing off in a variety of passive situations, for example, while watching television, sitting in a public place, lying down to rest (Johns, 1991). Higher scores indicate increased likelihood of falling asleep during passive activities. The possible range is 0-24, with a score >10 indicating "sleepy" and >18 indicating "very sleepy".

The Clinical Dementia Rating Scale (CDR) and the Neuropsychiatric Inventory (NPI) were collected at each annual PPG assessment. The CDR is used to stage the severity of dementia (Morris, 1993). The CDR rates performance in six areas of function (memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care) based on a semi-structured interview with an informant. A global score ranging from 0 (no dementia) to 3 (severe dementia) is computed. The CDR has been shown to be reliable with good levels of agreement among experienced investigators (Morris et al., 1997; Rockwood, Strang, MacKnight, Downer, & Morris, 2000). The NPI evaluates 12 neuropsychiatric symptoms common in dementia (delusions, hallucinations, agitation, depression, anxiety, apathy, irritability, euphoria, disinhibition, aberrant motor behavior, sleep disturbances, and appetite and eating abnormalities). The severity and frequency of each symptom is rated on the basis of scripted questions administered to the patient's caregiver with higher scores indicating greater behavioral symptomatology. Additionally, a score is calculated reflecting the emotional distress experienced by the caregiver related to the symptoms on a range from 0 (no distress) to 5 (very severely distressful) with higher scores indicative of greater emotional distress (Cummings, 1997).

The Mini-Mental State Examination (MMSE) is a 30-point brief cognitive rating screen. (Folstein, Folstein, & McHugh, 1975). The Geriatric Depression Scale (GDS) is a 30-item survey consisting of yes and no questions about how the respondent felt over the past week (Yesavage et al., 1983). Scores of 0-9 indicate normal mood, 10-19 indicate mild depression, and 20-30 indicate severe depression. The MMSE, CDR, and NPI were administered on the same day while the PSQI and ESS were completed during the actigraphy monitoring period.

Analysis

Actigraphy records were analyzed for both patient and caregiver at the medium sensitivity setting. Areas of validated “watch off” time were deleted from analysis as well as any periods greater than 2 hours when there was no recorded activity, indicating the watch was most likely off. Records for patient and caregiver were matched by deleting identical periods on both records to ensure accuracy in comparison. For example, if the patient had removed the watch one night, the data for both patient and caregiver were excluded for that night. To facilitate visual comparison the actogram activity scale was calibrated to be the same for all four data collection periods (Year 3 and 4 for both patient and caregiver). Average hourly activity scores were calculated and plotted for both patient and caregiver.

Within the 24-hour day there are three intervals of interest: active or daytime (from “lights on” in the morning to “lights off” at bedtime), rest or bedtime (from “lights off” to “lights on”), and the sleep interval that lies within the rest interval (the period between sleep start and sleep end). Due to the low overall activity of the patient, average activity per minute, percent immobility, number of immobility bouts, and immobility and mobility bout duration for active, rest, sleep, and 24-hour intervals were calculated. Sleep is determined by the software algorithm based on immobility parameters. Means were calculated for the following sleep interval variables: sleep duration, wake after sleep onset (WASO), sleep time, average sleep bout duration, and mobile time. Sleep efficiency is typically measured by the percent of sleep, normal being 85% of the sleep interval.

Circadian analyses to quantify both patient and caregiver 24-hour rest-activity rhythms were computed with nonparametric techniques. Nonparametric measures are sensitive to the characteristics of the empirical 24-hour activity profile. The following nonparametric rhythm outcome variables were calculated. Interdaily stability (IS) quantifies the degree of resemblance between activity patterns of individual days. Scores range theoretically between 0 and 1, with higher values reflecting a more stable and predictable rhythm. Intradaily variability (IV) is a measure of the fragmentation of periods of rest and activity. A typical 24-hour pattern demonstrates one prolonged activity period and one prolonged rest period. Values range theoretically between 0 and 2, with higher values indicating more fragmentation. Least active five hours (L5) is a measure of average activity during the 5 least active hours in the 24-hour average activity profile, indicating the trough of the rhythm. Conversely, M10 is the average activity during the sequence of the 10 most active hours in the 24-hour average activity profile, indicating the peak of the rhythm. The amplitude (AMP) gives the difference between the average activity level during M10 and L5. AMP is sensitive to overall level of activity; relative amplitude (RA) is calculated to obtain the normalized difference between the most active 10-hour period and the least active 5-hour period in an average 24-hour pattern. Dividing the AMP by the sum of L5 and M10 gives a value between 0 and 1, with higher numbers indicating a rhythm of higher amplitude or activity (Van Someren et al., 1999).

Magnetic resonance imaging (MRI) scans were obtained on a 1.5T Magnetom VISION system (Siemens, Iselin, NJ).

Results

Patient Characteristics

The patient experienced his first symptoms of FTD 3-4 years before he was evaluated, so he was likely in year 7-8 of disease when monitored with actigraphy. Descriptive data for the patient are summarized in Table 1. Over time there was an increase in dementia severity and a concomitant increase in cognitive impairment reflected by higher CDR and lower MMSE

scores. Scores on the ESS were high at Year 3 and increased at Year 4 reflecting higher probability of the patient falling asleep during passive activities. MRI scans (Figure 1) obtained at Year's 1, 2, and 3 illustrate the progression of the frontal lobe atrophy. The patient was unable to remain still for imaging at Year 4. Behavioral symptoms were assessed using the NPI each year for 4 years (Table 2). These data show that sleep complaints were not evident at Year 1, appeared by Year 2, and increased in severity and frequency in Years 3 and 4. There was an increase in apathy with advancing disease. Aberrant motor behaviors (compulsive and repetitive activities) are highest at Years 1 and 2, and diminished by Years 3 and 4. Agitation was present Year 1, diminished in Year 2, disappeared Year 3 and re-emerged in Year 4.

Twenty-four hour rest-activity data obtained from actigraphy are summarized in Table 3. Mobility bouts during the daytime were reduced from 4.8 minutes (Year 3) to 3.1 minutes (Year 4), and increased in the bedtime interval from 1.6 minutes (Year 3) to 4.0 minutes (Year 4). From Year 3 to 4, the number of immobility bouts had increased within all intervals, but the duration of the bouts shortened. The percent of immobility for active and rest intervals were similar, 55% and 51% respectively. Percent immobility within the sleep interval declined from 88 to 54%. Other changes in the sleep interval included a reduction in sleep time from 7.2 to 5.1 hours and a decrease in the percent of sleep from 90% (within normal limits) to 64% (below normal). Sleep variable data are illustrated on Figure 2. There is a decline in sleep duration, actual sleep time, and sleep bout duration while WASO and mobile time increase.

Circadian analysis (Table 4) shows a lack of stability from day to day (as measured by IS) at Year 3 with a pronounced decline by Year 4. The IV or within the day fragmentation was evident in Year 3 and worsened by Year 4. The L5 increases and the M10 decreases from Year 3 to 4. The amplitude of the rhythm was profoundly lower at Year 4 compared to Year 3 (measuring 55.59 at Year 3 and 13.77 at Year 4). The relative amplitude was markedly lower as well (measuring 0.70 at Year 3 and 0.14 at Year 4).

Caregiver Characteristics

The caregiver was a 53-year-old female in Year 3. She worked fulltime during the day, outside the home. At Year 3 patient and caregiver shared a bed; at Year 4 they slept in the same room but in different beds. At Year 3 the caregiver used sleeping medication (prescribed or over the counter) less than once a week; at Year 4 she reported no use of sleeping medications for the past month. In both years, her total PSQI score was 6 reflecting poor sleep quality, although her subjective rating of sleep quality was "fairly good". Emotional distress scores for behaviors endorsed on the NPI are shown in Table 2. Total distress scores were highest at time of diagnosis and remained relatively steady during subsequent years. Distress scores were highest for aberrant motor behaviors, disinhibition, and apathy. Emotional distress for apathy was highest at Year 1 and remained relatively stable over subsequent years. Ratings for emotional distress related to disturbances in the patient's sleep started in Year 2 and increased every year.

Twenty-four hour rest-activity data (Table 3) demonstrate mild changes between Year 3 and 4. Comparing Year 3 to 4, there is a decrease in activity counts per minute, and increase in percent immobility, number of immobility bouts, and immobility bout duration within the active interval. The percentage of sleep within the sleep interval remains normal during both years of monitoring (i.e., greater than 85%).

The sleep variables are shown in Figure 2. Sleep duration, sleep onset latency, sleep time, sleep bout duration were relatively unchanged. There was a mild decrease in WASO and mobile time at Year 4. Circadian data is reported on Table 4. These measures show a decline

in stability of from Year 3 to 4 (IS). In Year 4, the IV demonstrates an improved strength of her rhythm. L5 and M10 values remain stable over both years of monitoring. The amplitude and relative amplitude remain strong and change only minimally from Year 3 and Year 4.

Dyad Characteristics

Visual comparison of patient and caregiver actograms (Figure 3) reveals episodes of synchronized activity and nighttime interaction. During both years of monitoring the caregiver reports being awakened by the patient three times or more per week. The patient awakens the caregiver in order to say “hello” or to tell her he is getting up to the bathroom. Averages of hourly activity scores for the patient and caregiver (Figure 4) show daytime activity counts are much lower for the patient in both years.

Discussion

Data from multiples measures obtained in this study provide compelling evidence of profound rest-activity rhythm disturbances in this patient with FTD. The most remarkable finding is the extent of the decline in rhythm amplitude and relative amplitude, and decreased stability over time. Mobility bouts decreased in the daytime and increased in the nighttime; by Year 4 the patients' number of mobility bouts was higher at night than during the day. Immobility bout duration shortened over time, also reflecting increased fragmentation. These changes in movement during the active and rest intervals indicate a lack of identifiable 24-hour rest-activity rhythm. The IV (2.18) was higher than the typical range of 0-2 and is further evidence that WS had a highly fragmented rhythm. Past studies with institutionalized patients diagnosed with AD have not yielded impairment in stability, amplitude, and variability of this magnitude (Dowling et al., 2008), although one other study documents five institutionalized patients with advanced FTD who showed higher rhythm variability than patients with AD (Harper et al., 2001).

WS experienced profound changes in sleep. Sleep complaints were not voiced until Year 2 and then increased each year in frequency and severity. Time spent sleeping and the duration of sleep declined from Year 3 to 4, and by Year 4 sleep efficiency had dropped into the abnormal range. There was increased number of awakenings over time. A study of polygraphic sleep recordings from 12 patients with 8-year histories of symptoms of Pick's disease (a variant of FTD) also report reduction in total sleep time, increased awakenings, and other sleep stage disruption (Pawlak, 1986). The ESS scores suggest daytime issues as well in that the patient was more likely to doze off in passive situations.

Our findings emphasize the important role of frontal-subcortical circuits in governing drive, motivation, and activity. Ratings on the apathy scale of the NPI increased each year and correspond to the MRI findings of frontal atrophy. By Year 4, of all behavioral symptoms, apathy occurred most frequently. The plot of average hourly activity scores illustrates the flattened pattern of activity for the patient compared to his caregiver. The strongest zeitgebers that the patient has for his rest-activity rhythm are his caregiver's bedtime and rise times (0600 and 2200). The patient's apathy and low movement are reflected in the low amplitude of his rest-activity rhythm. The relationship between lowered movement and circadian function warrants future examination. For example, in non-demented subjects, circadian control of rest-activity rhythms was strengthened by engaging in a physical fitness protocol (Van Someren, Lijzenga, Mirmiran, & Swaab, 1997). In another study, restlessness and constant pacing was associated with improved stability and decreased fragmentation of circadian rhythm in an institutionalized patient with advanced Alzheimer's disease (Werth et al., 2002).

Dementias are associated with a myriad of behavioral symptoms that have a profound negative impact on the health and well-being of family caregivers (Ory, Hoffman, Yee, Tennstedt, & Schulz, 1999; Pruchno & Potashnik, 1989; Schulz, O'Brien, Bookwala, & Fleissner, 1995). Sleep disturbances are a major feature of the dementia caregiver experience (McCurry et al., 1999; Wilcox & King, 1999), are a source of significant caregiver burden and a primary reason for institutionalization (Ancoli-Israel, Klauber, Gillin, Campbell, & Hofstetter, 1994; Hope, Keene, Gedling, Fairburn, & Jacoby, 1998; Pollak & Perlick, 1991; Yaffe et al., 2002). This caregiver's distress about sleep-related issues increased each year. While research has demonstrated that caregivers may overstate their amount of sleep disturbance (McCurry, Vitiello, Gibbons, Logsdon, & Teri, 2006), this case study provides evidence that the caregiver's sleep was impacted by the patient's behavior. The interruptions by the patient were associated with poor sleep quality in the caregiver. It has been suggested that qualitative ratings of sleep may be influenced by caregiver fatigue and burden (McCurry, Gibbons, Logsdon, & Teri, 2004). In our clinical experience, caregivers report disturbed sleep secondary to anxiety and the need to be vigilant to patient needs during the night. These issues were not addressed in this study but warrant future exploration. Finally, despite the profound changes in the patient's rhythm, the caregiver's circadian rhythm and sleep parameters showed only mild changes and sleep efficiency remained in the normal range.

A limitation of this study is characterization of low activity levels in the patient. Raw activity counts are analyzed with an algorithm that differentiates sleep from wake based on movement. This algorithm may mistakenly score low activity as sleep. The ESS scores for this patient increased from Year 3 to 4, suggesting the patient was likely to doze during passive times but it is not clear whether the patient was sleeping or not.

Low activity can also be attributed to depression or apathy. The patient endorsed depressive symptoms at Year 1, but these complaints had diminished by Year 2 and 3. The caregiver endorsed mild depressive symptoms of the patient only at Year 4. Apathy and depression can be difficult to distinguish and the possibility exists that impaired cognition negatively impacts ability to self-report symptoms. In this case, actigraphic values of lower activity coincided with caregiver endorsements of apathy and the increased frontal atrophy seen on MRI. Thus, it is critical to augment actigraphy data with other measures in order to characterize the potential functional impacts of disturbed rest-activity rhythm.

There are other limitations to this study. While Tylenol PM and Benadryl were available as needed at Year 4, there was no documentation whether WS was taking these medications. Also, the disturbances evident in neurodegenerative conditions may be exacerbated by changes that occur with normal aging (Van Someren, 2000). Such changes affect sleep quality and include diminished sleep time, lower efficiency, increased nighttime awakening, and sleep fragmentation (Huang et al., 2002). It is not clear what impact these normal changes have on the data presented here. Finally, the suprachiasmatic nucleus (SCN), located in the anterior hypothalamus, has an established role in the regulation of circadian rhythms, but its potential influence on rest-activity alterations in FTD was not examined in this study.

Summary

This case demonstrates profound rest-activity disruption occurring in a patient with FTD. Rest-activity changes were evident in multiple aspects of the day and nighttime intervals. Actigraphy shows promise for characterizing rest-activity rhythms in patients with FTD and can be a useful adjunct to informant-based ratings. As patients with FTD typically have little to no insight into their condition (Mendez & Shapira, 2005; Rankin, 2005), such objective measures are an ideal way to obtain data. This case also characterizes aspects of the

caregiver experience relating to rest-activity changes in the patient and we demonstrate novel methods for illustrating the patient and caregiver interactions relating to day and night time activity. It is important to study rest-activity rhythms in FTD and to identify the point in the disease trajectory where disruption occurs. Further research may also help to clarify the functional impact of these disruptions. In this way, interventions can be developed aimed at minimizing the negative impact for both patients and their caregivers.

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References

- Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft W, Pollak CP. The role of actigraphy in the study of sleep and circadian rhythms. *Sleep* 2003;26(3):342–392. [PubMed: 12749557]
- Ancoli-Israel S, Klauber MR, Gillin JC, Campbell SS, Hofstetter CR. Sleep in non-institutionalized Alzheimer's disease patients. *Aging (Milano)* 1994;6(6):451–458. [PubMed: 7748919]
- Bathgate D, Snowden JS, Varma A, Blackshaw A, Neary D. Behaviour in frontotemporal dementia, Alzheimer's disease and vascular dementia. *Acta Neurologica Scandinavica* 2001;103(6):367–378. [PubMed: 11421849]
- Boeve BF, Silber MH, Ferman TJ, Kokmen E, Smith GE, Ivnik RJ, et al. REM sleep behavior disorder and degenerative dementia: an association likely reflecting Lewy body disease. *Neurology* 1998;51(2):363–370. [PubMed: 9710004]
- Brown AC, Smolensky MH, D'Alonzo GE, Redman DP. Actigraphy: a means of assessing circadian patterns in human activity. *Chronobiology International* 1990;7(2):125–133. [PubMed: 2242506]
- Brun A. Frontal lobe degeneration of non-Alzheimer type. I. Neuropathology. *Archives of Gerontology and Geriatrics* 1987;6(3):193–208. [PubMed: 3689053]
- Buyse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research* 1989;28(2):193–213. [PubMed: 2748771]
- Cummings J. The Neuropsychiatric Inventory: assessing psychopathology in dementia patients. *Neurology* 1997;48:S10–16. [PubMed: 9153155]
- Diehl J, Kurz A. Frontotemporal dementia: patient characteristics, cognition, and behaviour. *International Journal of Geriatric Psychiatry* 2002;17(10):914–918. [PubMed: 12325050]
- Dowling GA, Burr RL, Van Someren EJ, Hubbard EM, Luxenberg JS, Mastick J, et al. Melatonin and bright-light treatment for rest-activity disruption in institutionalized patients with Alzheimer's disease. *Journal of the American Geriatrics Society* 2008;56(2):239–246. [PubMed: 18070004]
- Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research* 1975;12(3):189–198. [PubMed: 1202204]
- Grace JB, Walker MP, McKeith IG. A comparison of sleep profiles in patients with dementia with lewy bodies and Alzheimer's disease. *International Journal of Geriatric Psychiatry* 2000;15(11):1028–1033. [PubMed: 11113983]
- Harper DG, Stopa EG, McKee AC, Satlin A, Fish D, Volicer L. Dementia severity and Lewy bodies affect circadian rhythms in Alzheimer disease. *Neurobiology of Aging* 2004;25(6):771–781. [PubMed: 15165702]
- Harper DG, Stopa EG, McKee AC, Satlin A, Harlan PC, Goldstein R, et al. Differential circadian rhythm disturbances in men with Alzheimer disease and frontotemporal degeneration. *Archives of General Psychiatry* 2001;58(4):353–360. [PubMed: 11296096]
- Hope T, Keene J, Gedling K, Fairburn CG, Jacoby R. Predictors of institutionalization for people with dementia living at home with a carer. *International Journal of Geriatric Psychiatry* 1998;13(10):682–690. [PubMed: 9818303]

- Huang YL, Liu RY, Wang QS, Van Someren EJ, Xu H, Zhou JN. Age-associated difference in circadian sleep-wake and rest-activity rhythms. *Physiology of Behavior* 2002;76(4-5):597–603.
- Ikeda M, Brown J, Holland AJ, Fukuhara R, Hodges JR. Changes in appetite, food preference, and eating habits in frontotemporal dementia and Alzheimer's disease. *Journal of Neurology, Neurosurgery, and Psychiatry* 2002;73(4):371–376.
- Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991;14(6):540–545. [PubMed: 1798888]
- Knopman DS, Petersen RC, Edland SD, Cha RH, Rocca WA. The incidence of frontotemporal lobar degeneration in Rochester, Minnesota, 1990 through 1994. *Neurology* 2004;62(3):506–508. [PubMed: 14872045]
- Langa KM, Chernew ME, Kabeto MU, Herzog AR, Ofstedal MB, Willis RJ, et al. National estimates of the quantity and cost of informal caregiving for the elderly with dementia. *Journal of General Internal Medicine* 2001;16(11):770–778. [PubMed: 11722692]
- Lindau M, Almkvist O, Kushi J, Boone K, Johansson SE, Wahlund LO, et al. First symptoms--frontotemporal dementia versus Alzheimer's disease. *Dementia and Geriatric Cognitive Disorders* 2000;11(5):286–293. [PubMed: 10940680]
- Littner M, Kushida CA, Anderson WM, Bailey D, Berry RB, Davila DG, et al. Practice parameters for the role of actigraphy in the study of sleep and circadian rhythms: an update for 2002. *Sleep* 2003;26(3):337–341. [PubMed: 12749556]
- Liu W, Miller BL, Kramer JH, Rankin K, Wyss-Coray C, Gearhart R, et al. Behavioral disorders in the frontal and temporal variants of frontotemporal dementia. *Neurology* 2004;62(5):742–748. [PubMed: 15007124]
- Marczinski CA, Davidson W, Kertesz A. A longitudinal study of behavior in frontotemporal dementia and primary progressive aphasia. *Cognitive and Behavioral Neurology* 2004;17(4):185–190. [PubMed: 15622012]
- McCurry SM, Gibbons LE, Logsdon RG, Teri L. Anxiety and nighttime behavioral disturbances. Awakenings in patients with Alzheimer's disease. *Journal of Gerontological Nursing* 2004;30(1):12–20. [PubMed: 14753054]
- McCurry SM, Logsdon RG, Teri L, Gibbons LE, Kukull WA, Bowen JD, et al. Characteristics of sleep disturbance in community-dwelling Alzheimer's disease patients. *Journal of Geriatric Psychiatry and Neurology* 1999;12(2):53–59. [PubMed: 10483925]
- McCurry SM, Vitiello MV, Gibbons LE, Logsdon RG, Teri L. Factors associated with caregiver reports of sleep disturbances in persons with dementia. *American Journal of Geriatric Psychiatry* 2006;14(2):112–120. [PubMed: 16473975]
- Mendez M, Shapira J. Loss of insight and functional neuroimaging in frontotemporal dementia. *Journal of Neuropsychiatry and Clinical Neurosciences* 2005;17(3):413–416. [PubMed: 16179666]
- Moore MJ, Zhu CW, Clipp EC. Informal costs of dementia care: estimates from the National Longitudinal Caregiver Study. *Journal Gerontology B Psychological Sciences Social Sciences* 2001;56(4):S219–228.
- Morris J. The Clinical Dementia Rating (CDR): current version and scoring rules. *Neurology* 1993;43:2412–2414. [PubMed: 8232972]
- Morris J, Ernesto C, Schafer K, Coats M, Leon S, Sano M, et al. Clinical dementia rating training and reliability in multicenter studies: the Alzheimer's Disease Cooperative Study experience. *Neurology* 1997;48(6):1508–1510. [PubMed: 9191756]
- Neary D, Snowden JS, Gustafson L, Passant U, Stuss D, Black S, et al. Frontotemporal lobar degeneration: a consensus on clinical diagnostic criteria. *Neurology* 1998;51(6):1546–1554. [PubMed: 9855500]
- Ory MG, Hoffman RR 3rd, Yee JL, Tennstedt S, Schulz R. Prevalence and impact of caregiving: a detailed comparison between dementia and nondementia caregivers. *Gerontologist* 1999;39(2):177–185. [PubMed: 10224714]
- Pawlak C, Blois R, Gaillard JM, Richard J. [Sleep in Pick disease] [Article in French]. *Encephale* 1986;12(6):327–334. [PubMed: 3816680]

- Pollak CP, Perlick D. Sleep problems and institutionalization of the elderly. *Journal of Geriatric Psychiatry and Neurology* 1991;4(4):204–210. [PubMed: 1789908]
- Pollak CP, Stokes PE. Circadian rest-activity rhythms in demented and nondemented older community residents and their caregivers. *Journal of the American Geriatrics Society* 1997;45(4):446–452. [PubMed: 9100713]
- Pollak CP, Stokes PE, Wagner DR. Nocturnal interactions between community elders and caregivers, as measured by cross-correlation of their motor activity. *Journal of Geriatric Psychiatry and Neurology* 1997;10(4):168–173. [PubMed: 9453684]
- Pruchno RA, Potashnik SL. Caregiving spouses. Physical and mental health in perspective. *Journal of the American Geriatrics Society* 1989;37(8):697–705. [PubMed: 2754154]
- Rankin K, B. E, Pace-Savitsky C, Kramer JH, Miller BL. Self awareness and personality changed in dementia. *Journal of Neurology, Neurosurgery, and Psychiatry* 2005;76(5):632–639.
- Ratnavalli E, Brayne C, Dawson K, Hodges JR. The prevalence of frontotemporal dementia. *Neurology* 2002;58(11):1615–1621. [PubMed: 12058088]
- Rockwood K, Strang D, MacKnight C, Downer R, Morris JC. Interrater reliability of the Clinical Dementia Rating in a multicenter trial. *Journal of the American Geriatrics Society* 2000;48(5):558–559. [PubMed: 10811551]
- Rosen HJ, Allison SC, Schauer GF, Gorno-Tempini ML, Weiner MW, Miller BL. Neuroanatomical correlates of behavioural disorders in dementia. *Brain* 2005;128(Pt 11):2612–2625. [PubMed: 16195246]
- Schulz R, O'Brien AT, Bookwala J, Fleissner K. Psychiatric and physical morbidity effects of dementia caregiving: Prevalence, correlates and causes. *Gerontologist* 1995;35:771–791. [PubMed: 8557205]
- Van Someren EJ. Circadian and sleep disturbances in the elderly. *Experimental Gerontology* 2000;35(9-10):1229–1237. [PubMed: 11113604]
- Van Someren EJ, Lijzenga C, Mirmiran M, Swaab DF. Long-term fitness training improves the circadian rest-activity rhythm in healthy elderly males. *Journal of Biological Rhythms* 1997;12(2):146–156. [PubMed: 9090568]
- Van Someren EJ, Swaab DF, Colenda CC, Cohen W, McCall WV, Rosenquist PB. Bright light therapy: improved sensitivity to its effects on rest-activity rhythms in Alzheimer patients by application of nonparametric methods. *Chronobiology International* 1999;16(4):505–518. [PubMed: 10442243]
- Volicer L, Harper DG, Manning BC, Goldstein R, Satlin A. Sundowning and circadian rhythms in Alzheimer's disease. *American Journal of Psychiatry* 2001;158(5):704–711. [PubMed: 11329390]
- Werth E, Savaskan E, Knoblauch V, Gasio PF, van Someren EJ, Hock C, et al. Decline in long-term circadian rest-activity cycle organization in a patient with dementia. *Journal of Geriatric Psychiatry and Neurology* 2002;15(1):55–59. [PubMed: 11936245]
- Wilcox S, King AC. Sleep complaints in older women who are family caregivers. *Journal of Gerontology B Psychological Sciences Social Sciences* 1999;54(3):P189–198.
- Witting W, Kwa IH, Eikelenboom P, Mirmiran M, Swaab DF. Alterations in the circadian rest-activity rhythm in aging and Alzheimer's disease. *Biological Psychiatry* 1990;27(6):563–572. [PubMed: 2322616]
- Yaffe K, Fox P, Newcomer R, Sands L, Lindquist K, Dane K, et al. Patient and caregiver characteristics and nursing home placement in patients with dementia. *Journal of the American Medical Association* 2002;287(16):2090–2097. [PubMed: 11966383]
- Yesavage J, Brink T, Rose T, Lum O, Huang V, Adey M, et al. Development and validation of a geriatric depression screening scale: a preliminary report. *Journal of Psychiatric Research* 1983;17:37–49. [PubMed: 7183759]
- Yesavage J, Friedman L, Kraemer HC, Noda A, Wicks D, Bliwise DL, et al. A follow-up study of actigraphic measures in home-residing Alzheimer's disease patients. *Journal of Geriatric Psychiatry and Neurology* 1998;11(1):7–10. [PubMed: 9686746]

Figure 1.
MRI, years 1, 2, and 3.

Figure 2.
Sleep interval mean values for patient (Pt) and caregiver (Cg).

Figure 3.
Interactions between patient and caregiver.

Figure 4.
Average hourly activity scores.

Table 1

Descriptive values for patient.

	CDR	MMSE	GDS	ESS (Average scores)
Year 1	1	27/30	11/30	Not done
Year 2	1	25/30	7/30	Not done
Year 3: Actigraphy	2	23/30	4/30	8
Year 4: Actigraphy	3	14/30	Unable to score	11.5

CDR, Clinical Dementia Rating Scale,

MMSE, Mini Mental State Examination,

GDS, Geriatric Depression Scale,

ESS, Epworth Sleepiness Scale

Table 2

Total and Caregiver Distress Scores from the Neuropsychiatric Inventory

NPI symptoms	Year 1 F × S	Caregiver Distress	Year 2 F × S	Caregiver Distress	Year 3 F × S	Caregiver Distress	Year 4 F × S	Caregiver Distress
Delusions	1	3	0	0	0	0	0	0
Hallucinations	0	0	0	0	0	0	3	0
Agitation	4	4	1	1	0	0	2	2
Depression	0	0	0	0	0	0	6	2
Anxiety	1	3	1	1	0	0	0	0
Euphoria	0	0	1	1	0	0	0	0
Apathy	8	4	8	2	12	3	12	2
Disinhibition	6	4	1	1	12	2	6	2
Irritability	6	3	0	0	0	0	0	0
Motor	12	5	12	2	8	3	4	1
Sleep	0	0	4	1	6	3	6	4
Eating	6	3	4	1	12	3	2	1
Totals	44	29	32	10	50	14	41	14

F (frequency) times **S** (severity) = Total score

Table 3

24-hour rest-activity data

Caregiver	Patient Year 3	Patient Year 4	Caregiver Year 3	Caregiver Year 4
24 hour Interval				
mean activity counts per min	51	52	136	126
day percent immobility	61%	55%	34%	36%
number of immobility bouts	144	203	101	109
mean immobility bout duration(min)	6.2	4.0	5.0	4.9
mean mobility bout duration (min)	3.9	3.3	9.4	9.1
Active Interval (daytime)				
mean activity counts per min	69	58	195	164
percent immobility	47%	55%	11%	14%
number of immobility bouts	106	134	54	61
mean immobility bout duration(min)	4.2	3.8	1.9	2.1
mean mobility bout duration(min)	4.8	3.1	16.1	15.0
Rest Interval (bedtime)				
mean activity counts per min	14	42	16	14
percent immobility	87%	51%	81%	84%
number of immobility bouts	41	66	46	42
mean immobility bout duration(min)	10.9	4.2	9.2	10.2
mean mobility bout duration(min)	1.6	4.0	1.9	1.8
Sleep Interval				
mean activity counts per min	13	41	14	13
percent immobility	88%	54%	83%	86%
number of immobility bouts	39	59	42	38
mean immobility bout duration(min)	11.2	4.5	9.8	11.3
mean mobility bout duration(min)	1.5	3.9	1.8	1.7
sleep time in hours	7.2	5.1	6.7	6.8
percent sleep	90%	64%	88%	89%

Min, minutes

Table 4

Circadian data

	PT Yr 3	PT Yr 4	CG Yr 3	CG Yr 4
IS (0-1)	0.45	0.17	0.47	0.30
IV (0-2)	1.76	2.18	0.80	0.37
L5	11.87	42.16	12.77	10.22
M10	67.46	55.93	195.72	199.11
Amp	55.59	13.77	182.95	188.89
RA	0.70	0.14	0.87	0.90

IS, interdaily stability

IV, intradaily variability

L5, least active 5 hours in the 24-hour period

M10, most active 10 hours in the 24-hour period

Amp, amplitude

RA, relative amplitude

PT, patient

CG, caregiver