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Tone Induced Sleep Fragmentation in Persons with Alzheimer's Disease: A Feasibility Study

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Abstract

Sleep fragmentation increases as Alzheimer's disease (AD) progresses and its effects on cognition, specifically vigilant attention, are profoundly important because vigilant attention is thought to be the first step in memory acquisition. To our knowledge, no one has experimentally studied the effect of sleep fragmentation on vigilant attention in persons with AD. Therefore, this study piloted an experimental method using sound (tones produced by an audiometer) to induce sleep fragmentation. Participants enrolled in the University of Arkansas for Medical Sciences Memory Research Center (MRC) ($n = 4$) underwent one night of undisturbed and one of fragmented sleep. We found that 100% of participants were able to tolerate the earphone needed for the tone-induced sleep fragmentation (TISF) method, and we were able to score awakenings in real time. However, only 50% of tones produced awakenings. The findings suggest that this experimental method is feasible for use in persons with mild AD. Based on the results we will increase the duration, intensity, and frequency of tones delivered for optimal result.

Keywords

Alzheimer's disease; dementia; attention; cognition; sleep fragmentation

Introduction

The incidence of Alzheimer's disease (AD) will increase to almost 1 million new cases annually by 2050 (Hebert, Beckett, Scherr, & Evans, 2001). Although prevention or cure for AD are important future goals, interventions are needed now for persons with AD and their caregivers to sustain their quality of life. In particular, stabilizing or slowing the progression of cognitive decline in those with AD could help maintain independence and delay admission to long-term care facilities. Therefore, we need to identify modifiable factors that could lead to interventions to slow cognitive decline. One potentially modifiable factor and a prominent clinical feature of AD that may influence cognitive decline is sleep fragmentation.

Nighttime sleep fragmentation and excessive daytime sleepiness often occur together; unlike persons with sleep deprivation (characterized by sleep deficit), persons with sleep fragmentation may have adequate time dedicated to sleep but experience frequent brief awakenings throughout the night. They may not be aware of these frequent brief awakenings, but they do know that their sleep is not refreshing and they experience excessive daytime sleepiness. In many cases, sleep fragmentation and daytime sleepiness increase as AD progresses in severity (Bliwise, Hughes, McMahon, & Kutner, 1995).

We know that sleep fragmentation and daytime sleepiness have significant adverse effects on vigilant attention in persons without AD (Bonnet, 1989; Edell-Gustafsson & Hetta, 2001; Kingshott, Cosway, Deary, & Douglas, 2000). Although the effects of sleep fragmentation on vigilant attention may also be important to persons with AD, the evidence for this is not conclusive. Research on persons with AD has sometimes not measured sleep objectively or controlled for important covariates. Further, we cannot assume that sleep fragmentation has the same effects on vigilant attention in persons with and without AD because the neuronal degeneration that characterizes AD may cause alterations in sleep-wake mechanisms (Everitt & Robbins, 1997; Szymusiak, 1995). Thus, we do not know whether sleep fragmentation has additive adverse effects on vigilant attention in AD or whether fragmentation of particular sleep stages affects vigilant attention. Clarification of these issues will help to determine whether improved sleep stabilizes or improves vigilant attention in persons with AD.

This pilot study tested the feasibility of using an experimental method to measure the effect of sleep fragmentation on vigilant attention in persons with AD. Specifically, the study used sound (tones sounded with an audiometer) to induce sleep fragmentation. Research questions were: 1) Will persons with AD tolerate the earphone needed for the tone induced sleep fragmentation (TISF) method? 2) Can a sleep technologist recognize electroencephalogram (EEG) awakenings and arousals after tones in real time? 3) What percent of tones produce an awakening according to EEG?

Materials and Methods

Study Design and Setting

We used a repeated measures design with one undisturbed and one fragmented night of sleep, (Figure 1) the study was conducted in the UAMS General Clinical Research Center (GCRC), which provided control of extraneous variables such as noise, visitors, and electrical interference that might introduce error in measurement and interpretation of the results. The Institutional Review Board and the Veterans Administration Research and Development Committee approved the study. The first author obtained informed consent from participants (and a legally authorized representative if it was determined that the person with AD was unable to provide informed consent). We obtained consent from participants at each stage of the study. Because of the possibility of temporary daytime sleepiness and cognitive status changes, a friend or family member was required to accompany participants throughout the study and drive them home.

Participants

We recruited a final sample of five participants, since this sample would be adequate to provide descriptive data on the TISF method.

Criteria for inclusion in this study were—(a) enrolled in UAMS Memory Research Center database; (b) consensus diagnosis: mild Alzheimer's disease (Clinical Dementia Rating = 1) (Morris, 1997) (Appendix 1). The consensus diagnosis is determined after extensive cognitive testing. A consensus committee consisting of behavioral neurologists, geriatrician, neurophysiologists, and nurses make the diagnosis according to criteria contained in the Diagnostic and Statistical Manual of Mental Disorders, Revised Fourth Edition, (American Psychiatric Association, 1994) and the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders criteria (McKhann et al., 1984). Participants also had to have a Mini Mental State Exam score ≥ 15 ; fewer than 10 respiratory sleep disturbances per hour during the first night of polysomnography; fewer than 5 leg movement sleep disturbances (periodic limb movement index with awakenings < 5) on the first night of polysomnography; self report of regular bedtime and wake time schedule (within 30 minutes) with at least 8 hours in bed for 5 days prior to the study; adequate hearing; on a consistent dose of a cholinesterase inhibitor or N-methyl-D-aspartic acid for seven days prior to the study or not receiving; an available family member or friend to stay with the participant in the GCRC.

Potential participants were excluded if there was self or family report of acute medical or psychological illness because acute medical or psychological illness could cause delirium, active hallucinations, and delusions and the TISF method could exacerbate these problems. The first author, an advanced practice nurse, screened the participant's hearing with a Maico MA 27 pure-tone audiometer. (American Speech-Language Hearing Association, 1997) If the participant's hearing was adequate, according to guidelines provided by the study audiologist, the participants were deemed able to continue in the study. Those on benzodiazepines and other hypnotics were also excluded because they could raise the threshold for awakening.

Description of Undisturbed Sleep and TISF Method

Undisturbed Sleep—We individualized bedtime and wake time according to the participant's usual hours of sleep. We determined their usual hours of sleep from a sleep diary that we requested the caregiver to keep for five days and nights prior to polysomnography. On Night 1, a registered polysomnographic technologist (RPSGT) conducted overnight polysomnography to acclimate participants to the procedure and screen for sleep disorders such as obstructive sleep apnea and periodic limb movement disorder. The RPSGT allowed participants to sleep undisturbed, and an insert earphone was positioned to accustom the participant to it.

The RPSGT used standard calibration and recording procedures as described in (Rechtschaffen A & Kales, 1968). Although, in April 2007, the American Academy of Sleep Medicine published "The AASM Manual for the Scoring of Sleep and Associated Events," meant to replace the R & K (1968) standard of sleep staging and unifying it with scoring roles for the most important events associated with sleep, at the time these data were collected the new criteria had not been published. Therefore, we utilized the R & K criteria with exceptions proposed by Dr. Bliwise, leading expert in sleep in persons with dementia (Bliwise, Willians, Irbe, Ansari, & Rye, 2000). Although rescoring the sleep studies with the new criteria might have resulted in changed results few reliability studies have been carried out at this time with the new criteria. Finally, because an important aspect of this feasibility study involved the ability to score sleep studies in real time to enable administration of the TISF method we determined that rescoring the sleep studies with the new criteria would not help us address the real time feasibility issue.

We used a Grass Portable Polysomnography Data Acquisition System (Astro-Med, Inc., West Warwick, RI) to measure sleep. The portable polysomnography system displays electrographically the electroencephalogram, electrooculogram, electromyogram, electrocardiogram, airflow, leg movement, respiratory excursion, and arterial oxygen saturation. Electroencephalographic electrodes were placed at C3, C4, O1, and O2 sites and referred to contralateral mastoid (A2, A1). Supplementary channels included nasal and oral thermistors to measure airflow, bilateral anterior tibialis myogram to measure leg movement, elastic bands on the chest and abdomen to measure respiratory excursion, and finger probe to measure oxygen saturation. The placement of EEG electrodes was performed in accordance with the international 10/20 system of electrode placement. (Jasper, 1958) Cleansing and application was performed in accordance with procedures outlined in *Sleep Disorders Medicine Second Edition*. (Keenan, 1999) Each electrode site was cleansed and lightly abraded with a gel based abrasive substance. Then scalp electrodes were firmly attached with collodion. We were careful to provide adequate ventilation when working with the collodion to prevent excessive accumulation of fumes. Because an air compressor was not available in the UAMS GCRC, we were not able to use an air compressor for quick drying. In situations where the air compressor is available we choose not to use this noisy equipment with persons with Alzheimer's disease due to our concern regarding participant anxiety. When the collodion was dry electrolyte gel was injected into the gold electrode cup using a blunt needle syringe. Electrode impedances were measured with an impedance meter and were below 5000 Ohms. Finally, at completion of electrode placement biological calibrations were performed to ensure accurate detection of electrical signals.

All sleep studies were scored by a RPSGT. All stage scoring was done using standardized scoring rules (American Academy of Sleep Medicine, 1999) with these two exceptions proposed by Dr. Bliwise—1) all non-rapid eye movement (NREM) stages were collapsed into 'indeterminate NREM sleep' because people with cognitive impairment have diffuse delta and theta activity; and 2) for people without rapid eye movement (REM) atonia, conventional scoring criteria for REM atonia were disregarded (Bliwise et al., 2000). The RPSGT received

training on scoring of sleep in cognitively impaired elders from Dr. Bliwise. Interscorer reliability of our RPSGT and Dr. Bliwise prior to beginning the study and quarterly during data collection ranged from .85–.95.

TISF Method—On Night 2, we individualized bedtime and wake time as we did on night 1. The RPSGT conducted overnight polysomnography using the standardized method previously described.

After we scored 10 minutes of sleep from the polysomnography tracing, the first author delivered tones with a Maico MA 27 pure-tone air conduction audiometer beginning at 5 dB (warble function) to induce an EEG scored awakening according to the exceptions outlined above (Figure 2). The RPSGT judged whether an awakening occurred. If there was no awakening, the first author increased the volume of the tone of 1000 Hz at 5-decibel intervals every 5 seconds until the participant awakened. When we scored an awakening, tone delivery stopped until the participant slept another 10 minutes and tone delivery resumed.

If we reached the 85-decibel ceiling limit without an EEG scored awakening, the first author entered the participant's room and called the participant's name. If the participant gave no response, the first author then gently touched the participant's arm. We noted a behavioral awakening when the participant gave an appropriate verbal response.

Rationale for TISF method (Frequency/Timing/Volume)—Awakenings were defined as a return to alpha/and or low voltage, mixed frequency activity rhythm lasting over half of one-30 second epoch. (Rechtschaffen A & Kales, 1968). Although in healthy persons, "Arousals are scored in REM sleep only when accompanied by concurrent increases in submental EMG amplitude." (1992) We scored wake based on return to alpha in our population with Alzheimer's disease (AD) (Bliwise et al., 2000). Because we have observed as few as 0–1 awakenings a night and as many as 16 awakenings in 30 minutes in persons with AD, we reviewed the literature for other studies using the TISF method to determine the most appropriate way to implement this method with our population. Other investigators have produced arousals as frequently as every 3–5 minutes to mimic the patterns of arousal seen in obstructive sleep apnea syndrome. (Martin, Brander, Deary, & Douglas, 1999; Martin, Engleman, Kingshott, & Douglas, 1997; Martin, Wraith, Deary, & Douglas, 1997) We chose tone delivery after 10 minutes of sleep to produce awakenings because this was less intrusive than the frequency used by Martin and his group, but still sufficiently frequent to clearly interrupt sleep and produce a measurable effect.

We chose a mid-range tone (1000 Hz.) audible to the majority of older adults (age-associated hearing loss is usually limited to higher range tones) (American Speech-Language Hearing Association, 1997). The initial volume was set at five decibels for 1 second. When the ceiling limit of 85 decibels was reached, a behavioral awakening was recorded. We used the ceiling limit of 85 decibels for 1 second recognized as safe by the American Academy of Audiology (American Academy of Audiology, 2003).

Variables and Their Measurement

We collected demographic data and a brief sleep history and evaluated baseline sleep with a self-report sleep log and nighttime polysomnography (night one in the GCRC). We then answered our feasibility questions with a log of descriptive information collected during the sleep studies.

Sleep—In addition to the nighttime sleep log, we used polysomnography to collect minutes of total sleep time, percent of night slept, minutes and percent of time awake, minutes of non-rapid eye movement sleep, minutes of rapid eye movement sleep, minutes to fall asleep (sleep

latency), and frequency of awakenings. When analyzing polysomnography data, initial scoring assigned a sleep stage (non rapid eye movement sleep [NREM] or stage 1,2,3,4 rapid eye movement [REM]) to each epoch (30-second segment of recording). After we scored each epoch for the entire recording, we calculated the total minutes of wake time and sleep time and thus were able to describe sleep by stage. We totaled awakenings and described them based on their cause (spontaneous, periodic limb movements of sleep, apneas, hypopneas, bathroom, tones, and behavioral), and also totaled the number of awakenings per hour of sleep.

Feasibility of the TISF Method—The first author and technologist checked the participant's ability to keep the earphone in place throughout the night. We also maintained a log of audiometer use that included the timing and loudness of tones required to wake participants and their responses. We compared the number of tones sounded to the number of awakenings, in real time. We then compared these notes to our review of polysomnography data to assess scoring accuracy.

Demographic Data—The first author used a standard form to collect data on age, diagnoses, medications, and descriptors of the sample. Scheduled medications were classified as: 1) cholinesterase inhibitors or N-methyl-D-aspartic acid, 2) sedating antidepressants, 3) anti-psychotics, 4) novel anti-psychotics, or 5) analgesics. We requested that the dosage of scheduled medications remain the same during the study unless a change was medically necessary and we monitored and recorded any changes.

Results

The goal of this small study was to establish the feasibility of the procedures, identify problem areas that needed modification, and provide preliminary estimates of standard deviations and correlation coefficients in longitudinal measurements.

Nine potential participants were recruited and 4 were enrolled in the study. Of the 5 who not enrolled, two were poor sleepers according to their sleep history, one had a cerebral hemorrhage before admission to the GCRC and one participant withdrew her consent after she learned that she could not smoke in the GCRC. One participant had an apnea/hypopnea index > 10 during the first night of polysomnography and was not able to complete two nights of PSG. Four participants completed two nights of PSG.

The final sample included 1 female and 3 males (Table 1). Their average age was 67.5 years (*SD* 11.03), with range from 51 to 74. All were Caucasian and had at least a high school education. Two participants had partially completed college and one had a graduate degree in education. Their mean MMSE score was 24.4 (*SD* 3.64), with scores ranging from 20–29, indicating mildly impaired cognitive status. All participants had a consensus diagnosis of mild Alzheimer's Disease (CDR = 1).

Measures of sleep continuity calculated from the undisturbed sleep night showed a mean sleep efficiency (ratio of time in bed to time asleep) of 66.2% (*SD* 13.01) with a range from 45% to 80.0% (Table 2). Healthy adults have an average sleep efficiency of about 95%. Total sleep time (TST) ranged from 242.5 minutes to 369.0 minutes, with a mean of 333.88 minutes (*SD* 61.20). Although all participants reported about 8 hours of sleep for 5 days prior to the study, during the study they only slept an average of 5.29 hours. On the first undisturbed night of sleep, participants awakened an average of 31 times. We found that on average, 18.4 awakenings were spontaneous and 9.2 awakenings were due to respiratory events.

Paired-sample *t* tests were conducted to evaluate whether there were significant differences between the undisturbed night of sleep and the TISF night. The number of sleep stage shifts

during the undisturbed night of sleep ($M = 72.00$, $SD = 24.34$) tended to be less than sleep stage shifts on the TISF night ($M = 102.75$, $SD = 18.75$), $t(3) = -2.51$, $p = .08$. Total awakenings also tended to differ between the undisturbed night of sleep ($M = 29.5$, $SD = 10.85$) and the TISF night ($M = 41.50$, $SD = 8.19$), $t(3) = -2.93$, $p = 0.06$.

We found that all (four) participants tolerated the earphone, and we were able to score awakenings and electroencephalogram arousals in real time and identify all non-rapid eye movement sleep stages. (Figure 2). About 50% of the tones resulted in an electroencephalogram scored awakening. All tones that resulted in awakenings were at the maximum 85-decibel level.

Discussion

Michael Bonnet developed the TISF method in an attempt to separate the confounded measurement of hypoxemia and sleep fragmentation in persons with obstructive sleep apnea (OSA). (Bonnet, 1985) When Bonnet was able to separate the effects of hypoxemia and sleep fragmentation ($n = 11$), he found that fragmented sleep had an additive adverse effect, on vigilant attention. (Bonnet, 1985) Findings by Martin and his group (Martin, Engleman, Deary, & Douglas, 1996) affirmed Bonnet's work. They found that one night of sleep fragmentation (without hypoxemia) made normal subjects sleepier during the day, impaired their subjective assessment of mood, and decreased their mental flexibility and vigilant attention. Here we sought to determine if Bonnet's method was feasible for use in persons with AD. Based on the results of this feasibility study, we will increase the duration, intensity, and frequency of tones delivered.

Recommendations for future TISF use

Because we found that sleep was severely disturbed by spontaneous awakenings on Night 1, we will add 1 night for acclimatization to the sleep laboratory to account for the first night effect. When people sleep in unfamiliar surroundings, such as a sleep laboratory, their sleep patterns may not be typical during the first night of change but may revert to patterns that are more usual on subsequent nights. In this study, we believe the setting enhanced the first-night effect.

Because participants had a shortened total sleep time and were essentially sleep deprived during their two nights in the GCRC, we believe our TSIF method was confounded by participants' sleep deprivation. In future studies we will control for lights out and rise time (10 PM–7 AM for all participants) to ensure an adequate time in bed and, minimize the effects of sleep deprivation.

Finally, because we found that sleep was disturbed due to respiratory events, although participants described themselves as good sleepers, we will the Epworth Sleepiness Scale and actigraphy instead of a subjective report of sleep. The Epworth Sleepiness Scale describes daytime sleepiness, which may help identify those with disrupted nighttime sleep. This simple questionnaire asks the respondents to rate the chance that they would doze off or fall asleep in eight situations commonly encountered in daily life, using a Likert scale. Total Epworth Sleepiness Scale scores have significantly distinguished normal participants from participants in various diagnostic groups including those with obstructive sleep apnea. (Johns, 1991) An actigraph is a small device that can be worn like a wrist watch for up to 3 weeks. The actigraph contains a piezoelectric cell that records participant movements, which are averaged over a predetermined period of time or epoch. The recordings can be downloaded to a computer where numerous parameters describing sleep/wake continuity can be calculated from an algorithm. The actigraph can thus provide objective proxy measures for total sleep time, total wake time, sleep efficiency, and other sleep continuity parameters.

In future studies sleep fragmentation will be defined as waking at least every 8 minutes after sleep onset. We will strive for an increased frequency of awakenings to ensure a significant difference in numbers of awakenings between the undisturbed and the TISF nights. Further, as described above we will add an additional night of acclimatization to account for first night effect. We will continue to define waking in two ways: 1) EEG scored wake and 2) behaviorally (appropriate verbal response). Although wake after sleep onset (WASO) provides one indicator of sleep fragmentation, we will continue to conceptualize sleep fragmentation as frequent, brief (8–13 minute) alternating periods of wake and sleep throughout the night. Based on the results of this feasibility study, we believe that number of awakenings is most descriptive of sleep fragmentation and behavioral state instability in this population.

Conclusion

Sleep fragmentation is a significant problem for persons with AD; it has more than one cause and has been defined in more than one way. Sleep fragmentation in people with AD may be conceptualized as frequent, brief (8–13 minute) alternating periods of wake and sleep throughout the night. To mimic this type of sleep fragmentation, the TISF method consists of experimental fragmentation of sleep after 8 minutes of undisturbed sleep. Eight minutes is less intrusive than the frequency used by other researchers but is likely to be sufficient produce a measurable effect. Although this study included only four participants with complete data, this preliminary work has demonstrated the feasibility of the proposed study methods in persons with mild Alzheimer's Disease.

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Steps	Frequency	Total
1. Recruitment and Initial screening Initial contact (Alzheimer's Disease Center staff contact). Informed consent process. Demographic data collection. Instruct in use of sleep log. Participants/family member will collect sleep log data.	1 Day 1 Day 6 Days	8 Days
2. Screening Participants to General Clinical Research Center. Evaluate sleep log. Hearing screen. Orientation to General Clinical Research Center. Collect polysomnography data on undisturbed night of sleep. Evaluate to determine if participants meet inclusion criteria <ul style="list-style-type: none"> • Apnea-Hypopnea Index ≤ 10 • Periodic Limb Movement Index with Awakenings ≤ 5. 	Day 1 Night 1	1 Day
3. TISF Method Participants remain in the GCRC. Polysomnography using TISF Method. Study Concludes	Day 2 Night 2	1 Day

Figure 1.
Study Overview

Figure 2.
Polysomnography Tracing Demonstrating Arousal after Tones.

Table 1

Participants Completing Two Nights of Polysomnography

Age	Gender	Education	Occupation	MMSE ^a
72	Male	Advanced Degree	High School Principal	24
74	Male	>12 years	Grocery Manager	27
51	Male	Partial College	Truck Driver	22
73	Female	High School	Bookkeeper	29

^a Mini Mental State Exam Score 0–30. Higher score indicates better cognitive status.

Table 2

Mean Sleep Characteristics (*n* = 4)

	Time in Bed ^a	Total Sleep Time ^b	Sleep Efficiency ^c	Total Wake Time ^d	Stage Shift ^e
Undisturbed Sleep (Night 1)	508.75	333.88	66.20%	165.00	72.00
TISF Method (Night 2)	465.75	322.13	69.75%	143.25	102.75

^aMinutes in bed.

^bMinutes asleep.

^cRatio of time in bed to time asleep.

^dMinutes of wake after sleep onset.

^eNumber of times participant shifts between sleep stages (Non rapid eye movement sleep stages 1–4 and rapid eye movement sleep)

Table 3

Nighttime Awakenings (*n* = 4)

	Spontaneous Awakenings	Respiratory Awakenings	TISF ^a Method	Behavioral Awakenings	Total Awakenings
Undisturbed Sleep (Night 1)	18.4	9.2	0	0	31
TISF Method (Night 2)	17.2	5.8	8.3	8.7	41.5

^aTone-induced sleep fragmentation method.

Appendix 1

Clinical Dementia Rating Stages (Morris, 1997)

Rating	Memory	Orientation	Judgement & Problem Solving	Community Affairs	Home & Hobbies	Personal Care
None 0	No memory loss or slight, inconsistent forgetfulness.	Fully oriented.	Solved everyday problems well, including financial and business affairs; judgement good in relation to past performance.	Independent function at usual level in job, shopping, volunteer, and social groups.	Life at home, hobbies, intellectual interests well maintained.	Fully capable of self-care.
Questionable 0.5	Consistent slight forgetfulness; partial recollection of event; "benign" forgetfulness.	Fully oriented except for slight difficulty with time relationships.	Slight impairment in solving problems, similarities, differences.	Slight impairment in these activities.	Life at home, hobbies, intellectual interests slightly impaired.	Full capable of self-care.
Mild 1	Moderate memory loss, more marked for recent events; defect interferes with everyday activities.	Moderate difficulty with time relationships; oriented for place at examination, may have geographic disorientation elsewhere.	Moderate difficulty in handling problems, similarities, differences; social judgement usually maintained.	Unable to function independently at these activities though may still be engaged in some; appears normal to casual inspection.	Mild but definite impairment of function at home; more difficult chores and more complicated hobbies & interests abandoned.	Needs prompting.
Moderate 2	Severe memory loss; only highly learned material retained; new material rapidly lost.	Severe difficulty with time relationships; usually disoriented in time, often place.	Severely impaired in handling problems, similarities, differences; social judgement usually impaired.	No pretense of independent function outside home; appears too ill to be taken to functions outside home.	Only simple chores preserved; very restricted interests, poorly sustained.	Requires assistance in dressing, hygiene keeping of personal effects.
Severe 3	Severe memory loss; only fragments remain.	Oriented to person only.	Unable to make judgements or solve problems.	No pretense of independent function outside home; appears too ill to be taken to functions outside home.	No significant function at home.	Requires much help with personal care; frequent incontinence.
Profound 4	Even fragments generally are lost; often unable to test memory because of unintelligible or irrelevant speech.	Occasionally responds to own name.	Unable to follow even simple instructions or commands.	Unable to participate meaningfully in any social setting.	Unable to engage meaningfully in any hobby or home activity.	May attempt to dress or feed self, non-ambulatory without assistance.
Terminal 5	No meaningful memory function; often uncomprehending or obtunded.	No recognition of self.	No awareness of problems or comprehension of surroundings.	Completely unable to engage in any activity.	Completely unable to engage in any activity.	Needs to be fed; bedridden.

Current staging of Dementia:

0 = No dementia

0.5 = Uncertain or deferred diagnosis

1 = Mild

- 2 = Moderate dementia
- 3 = Severe dementia
- 4 = Profound dementia
- 5 = Terminal dementia