

# A GUIDE to DEMENTIA DIAGNOSIS and TREATMENT

## From THE AMERICAN GERIATRICS SOCIETY

### INTRODUCTION

A 2010 report of the Alzheimer's Association estimates that one in eight, or 13 percent, of people over age 65 have Alzheimer's disease ([http://www.alz.org/alzheimers\\_disease\\_facts\\_figures.asp](http://www.alz.org/alzheimers_disease_facts_figures.asp)). The prevalence of Alzheimer's disease and other dementias will continue to increase with the rapid growth of our older population. Managing these complex conditions can be a challenge for busy practitioners. The American Geriatrics Society (AGS) is pleased to make this convenient guide on the Diagnosis and Treatment of Dementia available to healthcare providers and trainees who care for older adults.

This guide is based on two acclaimed AGS publications. *Geriatrics At Your Fingertips™* is a convenient, pocket-sized guide to the evaluation and management of diseases and disorders that most commonly affect older people. *The Geriatrics Review Syllabus: A Core Curriculum in Geriatric Medicine* is a comprehensive text for those who wish to expand and update their knowledge in the field.

The AGS is a nationwide, non-profit association of healthcare professionals dedicated to improving the health, independence, and quality of life for all older people. The AGS has a diverse, multidisciplinary membership of healthcare professionals, researchers, educators, administrators, and students. For more information on the AGS, its publications, and membership benefits, please go to [www.americangeriatrics.org](http://www.americangeriatrics.org) or call 800-247-4779.

### DEMENTIA SYNDROME

Chronic acquired decline in memory and in at least one other cognitive function (eg, language, visual-spatial, executive) sufficient to affect daily life.

### ESTIMATED FREQUENCIES OF DEMENTIA CAUSES

- AD: 60% – 70%
- Other progressive disorders: 15% – 30% (eg, vascular, Lewy body, frontotemporal)
- Completely reversible dementia (eg, drug toxicity, metabolic changes, thyroid disease, subdural hematoma, normal-pressure hydrocephalus): 2% – 5%

### RISK and PROTECTIVE FACTORS FOR DEMENTIA

#### Definite Risks

Age  
APOE4 (whites)  
Atrial fibrillation  
Depression  
Down syndrome  
Family history

#### Possible Risks

Delirium  
Head trauma  
Heavy smoking  
Hypercholesterolemia  
Hypertension  
Lower educational level  
Other genes  
Postmenopausal hormone therapy

#### Possible Protections

Currently there are no proven preventive measures to stop the onset of Alzheimer's disease. Antioxidants (eg, vitamin E, beta carotene) may provide possible protection. Use caution with vitamin E in those with cardiovascular disease because  $\geq 400$  IU may increase mortality.

### PROGRESSION OF ALZHEIMER'S DISEASE (AD)

**Mild Cognitive Impairment (preclinical)**  
**MMSE 26–30; CDR 0.5; FAST 3; MOCA < 26\***

- Report by patient or caregiver of memory loss
- Objective signs of memory impairment
- Mild construction, language, or executive dysfunction
- No functional impairment
- 6%–15% annual conversion rate to dementia syndrome
- Some cases of mild cognitive impairment may not progress to AD

**Early, Mild Impairment (yr 1–3 from onset of symptoms)**  
**MMSE 21–25; CDR 1; FAST 4\***

- Disoriented to date
- Naming difficulties (anomia)
- Recent recall problems
- Mild difficulty copying figures
- Problems managing finances
- Decreased insight
- Irritability, mood change
- Social withdrawal

**Middle, Moderate Impairment (yr 2–8)**  
**MMSE 11–20; CDR 2; FAST 5–6\***

- Disoriented to date, place
- Comprehension difficulties (aphasia)
- Impaired new learning
- Impaired calculating skills
- Getting lost in familiar places
- Problems with dressing, grooming
- Not cooking, shopping, banking
- Restless, anxious, depressed
- Delusions, agitation, aggression

**Severe Impairment (yr 6–12)**  
**MMSE: 0–10; CDR 3; FAST 7\***

- Remote memory gone
- Nearly unintelligible verbal output
- Unable to copy or write
- No longer grooming or dressing
- Incontinent
- Motor or verbal agitation
- Distressing conditions common in advanced dementia include pressure ulcers, constipation, pain, and shortness of breath
- Among nursing home residents with advanced dementia, 71% die within 6 months of admission

\* MMSE = Mini-Mental State Examination; CDR = Clinical Dementia Rating Scale; FAST = Reisberg Functional Assessment Staging Scale; MoCA = Montreal Cognitive Assessment

### NEUROPSYCHIATRIC SYMPTOMS

Consider superimposed delirium or pain as precipitating factor.

#### Psychotic Symptoms (eg, delusions, hallucinations)

- Seen in about 20% of AD patients
- Delusions may be paranoid (eg, people stealing things, spouse unfaithful)
- Hallucinations (~11% of patients) are more commonly visual

#### Depressive Symptoms

- Seen in up to 40% of AD patients; may precede onset of AD
- May cause acceleration or decline if untreated; suspect if patient stops eating or withdraws
- Sadness
- Loss of interest in usual activities
- Anxiety and irritability

#### Apathy

- High prevalence and persistence throughout course of AD
- Causes more impairment in ADL than expected for cognitive status
- High overlap with depressive symptoms but lacks depressive mood, guilt, and hopelessness

#### Agitation or Aggression

- Seen in up to 80% of patients with AD
- A leading cause of nursing-home admission



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## EVALUATION

**History:** Always obtain from family or other caregiver: time symptoms first noted, family history of dementia, head injury, falls, alcohol and other substance exposure, history of depression, focal weakness, gait disturbance.

**Comprehensive physical and neurologic examination:** Check esp. for focal weakness, gait impairment, language impairment, extrapyramidal signs (rigidity, tremor, bradykinesia).

**Assess functional status:** Ask about bathing, dressing, toileting, transferring, as well as intermediate activities (eg, managing finances, medications, cooking, shopping).

**Evaluate mental status** for attention, immediate and delayed recall, remote memory, executive function, depression. Useful screening tests are the Mini-Cog, number of animals named in 1 minute (18 is average; less than 10 markedly abnormal), MMSE, Geriatric Depression Scale, PHQ-9. If Mini-Cog is positive, use MMSE (<http://www.minimental.com>) or Montreal Cognitive Assessment (<http://www.mocatest.org>).

*Note:* The MMSE is not as accurate in individuals with less than an 8th-grade education, or in those from varied cultural backgrounds or whose primary language is not English (higher rates of false positives). It is also not sensitive in highly educated individuals, although a score of 30 can still indicate cognitive impairment. The Mini-Cog or MOCA may be more appropriate to use in these instances.

### Clinical Features Distinguishing AD and Other Dementias

**AD:** Memory, language, visual-spatial disturbances, indifference, delusions, agitation

**Frontotemporal dementia:** Relative preservation of memory and visual-spatial skills, personality change, executive dysfunction, excessive eating and drinking

**Lewy body dementia:** visual hallucinations, delusions, extrapyramidal symptoms, fluctuating mental status, sensitivity to antipsychotic medications

**Vascular dementia:** abrupt onset, stepwise deterioration, executive dysfunction, gait changes

### Neuropsychological Testing

Reference standard for the presence of dementia or mild cognitive impairment:

- Especially helpful in mild, early disease and atypical presentations
- Quantifies and establishes the type of cognitive deficits
- Establishes baseline for comparison

### Laboratory Testing

- Complete blood cell count, thyroid-stimulating hormone, B<sub>12</sub>, folate, serum calcium, liver and kidney function tests, electrolytes
- Serologic test for syphilis (selectively)
- Glucose and HIV for patients at risk
- Genetic testing and “Alzheimer blood tests” are not currently recommended for clinical use.

### Neuroimaging (MRI or CT of the Brain)

- The likelihood of detecting structural lesions is increased with:
  - Onset age <60 years
  - Focal (unexplained) neurologic signs or symptoms
  - Abrupt onset or rapid decline (weeks to months)
  - Predisposing conditions (eg, metastatic cancer or anticoagulants)
- Neuroimaging may detect the 5% of patients with clinically significant structural lesions that would otherwise be missed.
- FDG-PET scans approved by Medicare for atypical presentation of course of AD in which frontotemporal dementia diagnosis is suspected. See [http://www.petscaninfo.com/portals/pat/medicare\\_guidelines\\_alzheimers](http://www.petscaninfo.com/portals/pat/medicare_guidelines_alzheimers)

## DIAGNOSIS OF AD

- Dementia syndrome
- Gradual onset and continuing decline
- Not due to another physical, neurologic, or psychiatric condition or to medications
- Deficits not seen exclusively during delirium

## TREATMENT

Primary goals are to improve quality of life and maximize functional performance by enhancing cognition and addressing mood and behavior. Although completely reversible dementia (eg, drug toxicity) is rare, identifying and treating secondary physical conditions may improve function.

### General Treatment Principles

- Identify and treat comorbid physical illnesses (eg, hypertension, diabetes mellitus)
- Promote brain health by exercise, balanced diet, stress reduction
- Avoid anticholinergic medications, eg, benztrapine, diphenhydramine, hydroxyzine, oxybutynin, tricyclic antidepressants, clozapine, thioridazine
- Limit prn psychotropic medication use
- Specify and quantify target behaviors
- Set realistic goals
- Maximize and maintain functioning
- Assess and monitor psychiatric status
- Intervene to decrease hazards of wandering
- Monitor physical environment for safety (eg, stairs)
- Advise patient and family concerning driving
- Establish and maintain relationship with patient and family
- Advise patient and family about sources of care and support, financial and legal issues, and advance directives, including establishing surrogate decision maker
- Consider referral to hospice (Reisberg Functional Assessment Staging (FAST) Scale = 7)

### Nonpharmacologic Approaches

Advise caregiver(s) to:

- Use scheduled toileting and prompted toileting for incontinence.
- Offer graded assistance (as little help as possible to perform ADLs), role modeling, cueing, and positive reinforcement to increase independence.
- Avoid adversarial debates; try to redirect conversation instead.
- Maintain a calm demeanor.
- Use services of caregiver support groups.

For problem behaviors:

- Music during meals, bathing
- Walking or light exercise
- Simulate family presence with video or audio tapes
- Pet therapy
- Speak at patient’s comprehension level
- Bright light, “white” noise (ie, low-level, background noise)

### Pharmacologic Treatment of Cognitive Dysfunction

- Patients with mild or moderate Alzheimer’s disease (AD) should receive a trial of a cognitive enhancer (**Table 1**).
- Because the effects of treatment cannot be fairly evaluated until the patient has been on a cognitive enhancer for some time, caregivers should commit to a trial treatment period of at least 3 months before the medication is started.
- In controlled trials, modest symptomatic benefit for cognition, mood, behavioral symptoms, and daily function was seen in patients with AD treated for 1 year with cholinesterase inhibitors versus placebo; open trials demonstrated benefit for 3 yr.
- Only 10%–25% of patients taking cholinesterase inhibitors may show modest global improvement, but more patients may have less rapid cognitive decline.
- Initial studies have shown benefits of these medications for patients with dementia associated with Parkinson’s disease, Lewy body dementia, and vascular dementia.
- Cholinesterase inhibitors have not been convincingly demonstrated to slow progression of mild cognitive impairment to dementia, but early treatment may help maintain function at higher level for longer periods.
- Cholinesterase inhibitors may attenuate noncognitive symptoms and delay nursing-home placement.
- Memantine (*Namenda*) demonstrated modest efficacy compared with placebo in moderate to severe AD as monotherapy and when combined with donepezil (*Aricept*).
- D/C cognitive enhancers when FAST=7.
- Vitamin E @1000 IU q12h found to delay functional decline in AD (caution in those with cardiovascular disease because ≥400 IU may increase mortality).
- *Ginkgo biloba* is not generally recommended.
- *Axona* (medium-chain triglyceride) has insufficient evidence to support its value in preventing or treating AD, and long-term effects are uncertain.

**Table 1. Cognitive Enhancers**

Medication	Dosage
Donepezil ( <i>Aricept</i> ) <sup>a, b</sup>	Start at 5 mg/d, increase to 10 mg/d after 1 mo; must be on 10 mg/d for at least 3 mo to consider increasing to 23 mg/d
Galantamine ( <i>Razadyne</i> ) <sup>a, c</sup> ( <i>Razadyne ER</i> ) <sup>a, c</sup>	Start at 4 mg q12h, increase to 8 mg q12h after 4 wk; recommended dosage 8 or 12 mg q12h
Rivastigmine ( <i>Exelon</i> ) <sup>a</sup>	Start at 1 capsule daily, preferably with food; titrate as above
Rivastigmine ( <i>Exelon</i> ) <sup>a</sup>	Start at 1.5 mg q12h and gradually titrate up to minimally effective dosage of 3 mg q12h; continue up to 6 mg q12h as tolerated; for patch, start at 4.6 mg/d, may be increased after ≥4 wk to 9.5 mg/d (recommended effective dosage); retitrate if medication is stopped
Memantine ( <i>Namenda</i> [NMDA antagonist]) <sup>b</sup>	Start at 5 mg/d, increase by 5 mg at weekly intervals to max of 10 mg q12h; if CrCl <30mL/min, max dose is 5 mg q12h

<sup>a</sup> Cholinesterase inhibitors. FDA labeling for AD is as follows: donepezil—mild, moderate, severe; galantamine—mild, moderate; rivastigmine—mild, moderate. Continue if patient improves or stabilizes; stopping medication can lead to rapid decline. Adverse events increase with higher dosage. Possible adverse events include nausea, vomiting, diarrhea, dyspepsia, anorexia, weight loss, leg cramps, bradycardia, syncope, insomnia, and agitation.

<sup>b</sup> Approved by FDA for moderate to severe AD. Possible adverse events include dizziness, headache, somnolence. NMDA = N-methyl-d-aspartate.

<sup>c</sup> Increased mortality found in controlled studies of mild cognitive impairment.

**Evaluation of Response to Any Cognitive Enhancer**

- Elicit caregiver observations of patient’s cognitive function and behavior (alertness, initiative) and follow functional status (ADLs and instrumental ADLs).
- Follow cognitive status (eg, improved or stabilized) by caregiver’s report or serial ratings of cognition (eg, Mini-Cog, MMSE).

**Treatment of Agitation**

- Consider nonpharmacologic approaches first.
- Identify and examine context of behavior (is it harmful to patient or others?) and environmental triggers (eg, overstimulation, unfamiliar surroundings, frustrating interactions).
- Are delusions or hallucinations interfering with function?
- Exclude underlying physical discomfort (eg, illnesses or medications).
- For intermittent disruptive behaviors (once per week or less), identifying antecedents of the behavior and avoiding triggers is often most useful. Behavior modification using positive reinforcement of desirable behavior has been shown to be effective, and also helps caregiver focus on times when behavior is not a problem.
- Physical restraint in any form should be avoided if at all possible. If restraining measures are necessary, careful supportive care should be provided to the patient. Over time, it is usually possible to reduce or eliminate the amount of restraint.
- Select pharmacologic agent on the basis of symptoms (**Table 2**).
  - Cognitive enhancers may slow deterioration, and agitation may worsen if they are discontinued.
  - Low dosages of antipsychotic medications have a limited role but may be necessary at times. *Note:* this use is “off label”; use in AD patients has a BLACK BOX warning because the risk of death was higher with drug treatment than with placebo in clinical trials. Risk–benefit must be discussed with both patients and caregivers before starting treatment. In the CATIE-AD trial (*NEJM* 2006;355:1525–1538), modest treatment with second-generation antipsychotics showed no significant benefit (p=0.22). Olanzapine, risperidone, and quetiapine had marginally higher response rates (32%, 29%, and 26%, respectively) than placebo (21%). Response was mitigated by greater extrapyramidal symptoms, sedation, and confusion in the treated groups. Weight gain was reported, particularly in women treated with olanzapine and quetiapine. Olanzapine was also associated with decreased HDL cholesterol.

**Table 2. Pharmacologic Treatment of Agitation**

Symptom	Medication and Usual Dosing
Agitation in context of nonacute psychosis	Aripiprazole 2.5–12.5 mg/d <sup>a</sup> Olanzapine 2.5–10 mg/d <sup>a</sup> Quetiapine 12.5–100 mg/d <sup>a</sup> Risperidone 0.25–3 mg/d <sup>a</sup> SSRI, eg, citalopram 10–30 mg/d
Agitation in context of depression	
Anxiety, mild to moderate irritability	Buspirone 15–60 mg/d <sup>b</sup> Trazodone 50–100 mg/d <sup>c</sup>
Agitation or aggression unresponsive to first-line treatment	Carbamazepine 300–600 mg/d <sup>d</sup> Divalproex sodium 500–1500 mg/d <sup>e</sup> Olanzapine (intramuscular) 2.5–5 mg IM <sup>a, f</sup>
Sexual aggression, impulse-control symptoms in men	Second-generation antipsychotic or divalproex (see dosages above) If no response, conjugated equine estrogens 0.625–1.25 mg/d <b>or</b> medroxyprogesterone injectable 100mg/wk IM

<sup>a</sup> Greater mortality and cerebrovascular events than placebo; use with particular caution in patients with cerebrovascular disease or hypovolemia.

<sup>b</sup> Can be given q12h; allow 2–4 wk for adequate trial.

<sup>c</sup> Small divided daytime dosage and larger bedtime dosage; watch for sedation and orthostasis.

<sup>d</sup> Monitor serum levels; periodic CBCs, platelet counts secondary to agranulocytosis risk. Beware of drug-drug interactions.

<sup>e</sup> Can monitor serum levels; usually well tolerated; check complete blood count (CBC), platelets for agranulocytosis, thrombocytopenia risk.

<sup>f</sup> For acute use only; initial dose 2.5–5mg, second dose (2.5–5mg) can be given after 2 hr, maximum of 3 injections in 24 hr (maximum daily dose 20mg); should not be administered for more than 3 consecutive days.

**FDA Advisory Information on Second-generation Antipsychotics**

In 17 randomized, controlled trials in which 5106 older adults with dementia-related behavioral disorders were enrolled, the risk of death in the drug-treated patients was 1.6–1.7 compared with that of the placebo group. Treatments consisted of *Zyprexa* (olanzapine), *Abilify* (aripiprazole), *Risperdal* (risperidone), or *Seroquel* (quetiapine). These trials averaged about 10 weeks. The rate of death was about 4.5% in drug-treated patients and about 2.6% in the placebo group. Most of the deaths appeared to be either cardiovascular (eg, heart failure, sudden death) or infectious (eg, pneumonia) in nature.

**CAREGIVER ISSUES AND RESOURCES**

- Maintaining the health and well-being of caregivers is essential for effective treatment of dementia patients.
- Over 50% of caregivers develop depression.
- Physical illness, isolation, anxiety, and burnout are common.
- Intensive education and support of caregivers may delay institutionalization of patients with dementia.
- Adult day services for patients and respite services for caregivers may help.
- Alzheimer’s Association (<http://www.alz.org> / 800-272-3900) offers education and support services (eg, Safe Return; chapters are located in major cities throughout US).
- Family Caregiver Alliance (<http://www.caregiver.org> / 800-445-8106) offers support, education, and information for caregivers.

**REFERENCES**

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Lantz MS, Khanmohamadi A, Wong PY. Behavioral problems in dementia. In: Pacala JT, Sullivan GM, eds. *Geriatrics Review Syllabus: A Core Curriculum in Geriatric Medicine*. 7<sup>th</sup> ed. New York: American Geriatrics Society; 2010:285-294.

Reuben DB, Herr KA, Pacala JT, Pollock BG, Potter JF, Semla TP. Dementia. In: *Geriatrics At Your Fingertips*. 2011. 13<sup>th</sup> ed (in production). New York: The American Geriatrics Society.



### Mini-Cog™ Screen for Dementia

The Mini-Cog™ screen combines an uncued 3-item recall test with a clock-drawing test (CDT) that serves as a recall distractor. The Mini-Cog can be administered in about 3 min, requires no special equipment, and is less influenced by level of education or language differences.

#### Administration

1. Make sure you have the patient's attention. Instruct the patient to listen carefully to, repeat back to you, and remember (now and later) 3 unrelated words. You may present the same words up to 3 times if necessary.
2. Instruct the patient to draw the face of a clock, either on a blank sheet of paper, or on a sheet with the clock circle already drawn on the page. After the patient puts the numbers on the clock face, ask him or her to draw the hands of the clock to read a specific time (11:10 or 8:20 are most commonly used; however, other times that require use of both halves of the clock face may be effective). These instructions can be repeated, but no additional instructions should be given. If the patient cannot complete the CDT in 3 min or less, move on to the next step.
3. Ask the patient to repeat the 3 previously presented words.

#### Scoring

- Give 1 point for each recalled word after the CDT distractor. Score 0–3 for recall.
- Give 2 points for a normal CDT, and 0 points for an abnormal CDT. The CDT is considered normal if all numbers are depicted, once each, in the correct sequence and position, and the hands readably display the requested time. Do not count equal hand length as an error. Add the recall and CDT scores together to get the Mini-Cog score:
- 0–2 positive screen for dementia
  - 3–5 negative screen for dementia

Source: Adapted from Borson S, Scanlan J, Brush M, Vitaliano P, Dokmak A. The Mini-Cog: a cognitive "vital signs" measure for dementia screening in multi-lingual elderly. *Int J Geriatr Psychiatry* 2000; 15(11):1021–1027, and Borson S, Scanlan JM, Watanabe J, Tu SP, Lessig M. Improving identification of cognitive impairment in primary care. *Int J Geriatr Psychiatry* 2006; 21(4):349–355. Reprinted with permission of S. Borson. Mini-Cog™ Copyright 2000, 2006, 2007. All rights reserved. Licensed for print distribution by S. Borson, MD, solely use as a clinical aid. Any other use is strictly prohibited. To obtain information on the Mini-Cog™ contact Dr. Borson at [soob@u.washington.edu](mailto:soob@u.washington.edu).

### Geriatric Depression Scale (GDS, Short Form)

Choose the best answer for how you felt over the past week.

1. Are you basically satisfied with your life? **yes/no**
2. Have you dropped many of your activities and interests? **yes/no**
3. Do you feel that your life is empty? **yes/no**
4. Do you often get bored? **yes/no**
5. Are you in good spirits most of the time? **yes/no**
6. Are you afraid that something bad is going to happen to you? **yes/no**
7. Do you feel happy most of the time? **yes/no**
8. Do you often feel helpless? **yes/no**
9. Do you prefer to stay at home, rather than going out and doing new things? **yes/no**
10. Do you feel you have more problems with memory than most? **yes/no**
11. Do you think it is wonderful to be alive now? **yes/no**
12. Do you feel pretty worthless the way you are now? **yes/no**
13. Do you feel full of energy? **yes/no**
14. Do you feel that your situation is hopeless? **yes/no**
15. Do you think that most people are better off than you are? **yes/no**

#### Scoring

Score 1 point for each bolded answer.  
Cut-off: normal 0–5; above 5 suggests depression.

Source: Courtesy of Jerome A. Yesavage, MD. For 30 translations of the GDS, see [www.stanford.edu/~yesavage/GDS.html](http://www.stanford.edu/~yesavage/GDS.html)

For additional information on administration and scoring, refer to the following references:

Sheikh JJ, Yesavage JA. Geriatric Depression Scale: recent evidence and development of a shorter version. *Clin Gerontol* 1986;5:165–172.

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### Reisburg Functional Assessment Staging (FAST) Scale

This 16-item scale is designed to parallel the progressive activity limitations associated with AD. Stage 7 identifies the threshold of activity limitation that would support a prognosis of 6 mo or less remaining life expectancy.

#### FAST

##### Activity Limitation Associated with AD

Stage	Activity Limitation Associated with AD
Stage 1	No difficulty, either subjectively or objectively
Stage 2	Complaints of forgetting location of objects; subjective work difficulties
Stage 3	Decreased job functioning evident to coworkers; difficulty in traveling to new locations
Stage 4	Decreased ability to perform complex tasks (eg, planning dinner for guests, handling finances)
Stage 5	Requires assistance in choosing proper clothing
Stage 6	Decreased ability to dress, bathe, and toilet independently
	Substage 6a Difficulty putting clothing on properly
	Substage 6b Unable to bathe properly, may develop fear of bathing
	Substage 6c Inability to handle mechanics of toileting (ie, forgets to flush, does not wipe properly)
	Substage 6d Urinary incontinence
	Substage 6e Fecal incontinence
Stage 7	Loss of speech, locomotion, and consciousness
	Substage 7a Ability to speak limited (1–5 words a day)
	Substage 7b All intelligible vocabulary lost
	Substage 7c Nonambulatory
	Substage 7d Unable to smile
	Substage 7e Unable to hold head up

Source: Reisberg, B. Functional assessment staging (FAST). *Psychopharmacol Bull* 1988;24(4):653–659. Copyright MedWorks Media Global, LLC. Reprinted with permission.