

Agitation

How to manage behavior disturbances in the older patient with dementia

Judith Neugroschl, MD

Behavior disturbances are common among persons with dementia and can be clinically challenging to manage. Delusions and hallucinations, aggression and combativeness, sleep disorders, anxiety, and depression—collectively characterized as agitation—are among the commonly occurring behavioral problems affecting persons with dementia. Agitation can be precipitated by undiagnosed medical problems or pain, drug interactions, environmental or social triggers (unpleasant experiences, overstimulation, unwanted care), poor sleep, delirium, and depression. Effective management involves behavioral assessment and pharmacotherapy with antipsychotics (neuroleptics), antidepressants, and mood stabilizers.

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Behavior disturbances are common in older persons with dementia, occurring in up to 50% of community-dwelling patients and 70 to 90% of nursing home patients with Alzheimer's disease (AD).¹ Behavior and pharmacologic management can improve the quality of life for patient and caregiver and may delay nursing home placement.² Although behavior disturbances may worsen with disease progression, symptoms may not be present on every examination.

This article discusses the issues in-

involved in diagnosing and managing behavior disturbance in dementia. Two tables list common behavior disturbances and triggers; a third table summarizes dosing recommendations for pharmacotherapy.

Common disturbances

Behavior disturbances can take many forms (table 1) and are often collectively referred to as agitation. Examples include wandering, purposeless activity, resistance to care, and self-injury. In general, agitation that occurs in response to care (dressing, bathing) causes the most distress for patients and their caregivers.

Pathophysiology

The pathophysiology of behavior disturbance in dementia is poorly understood. Restlessness may be associated with abnormalities in the striatum, cor-

tex, and thalamus, and be partially mediated by gamma-aminobutyric acid (GABA).³

Patients with dementia and agitation may have lower than normal levels of serotonin, with increased postsynaptic receptor sensitivity.⁴ Studies using functional neuroimaging suggest that frontal and temporal lobe pathology is associated with agitation and particularly psychosis.⁵ In addition, psychosis has been associated with significantly increased amounts of amyloid plaques in the prosubiculum and increased amounts of neurofibrillary tangles in the middle frontal cortex.⁶

Diagnosis

The first step of the work-up is to rule out a physical cause. Agitation can be precipitated by a medication (adverse drug reaction or drug-drug interaction) or substance intoxication or withdrawal. Delirium, pain syndromes, infection, bladder distention, and fecal impaction can cause agitation, exacerbate it, or lead to dementia-related agitation. Because patients with dementia often have trouble expressing themselves with words, common medical conditions or pain can go undiagnosed:

- Patients with moderate dementia who have undergone surgery may be in pain but unable to verbalize the need for PRN analgesic therapy. Their pain

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Table 1 Behavior disturbances (agitation)

Wandering	Disrobing
Pacing	Sexually inappropriate gestures or comments
Purposeless behaviors*	Disinhibition
Irritability	Cursing
Hitting, biting, yelling, threatening	Self injury (head banging, scratching)
Angry outbursts	Paranoia
Sleep-wake disturbances	Visual and/or auditory hallucinations
Anxiety	Hyperorality
Restlessness	Resistance to care†
“Sundowning”	

* Packing, opening/closing drawers, hoarding

† Combative behavior during bathing and dressing)

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may be expressed as agitation. This problem can be addressed by issuing standing orders for analgesic therapy.

- Patients with an exacerbation of congestive heart failure or chronic obstructive pulmonary disease may be uncomfortable, hypoxemic, or confused, any of which can result in agitation.

- Patients with dementia may not ask for fluids and become dehydrated, which can lead to delirium.

- Changes in renal or hepatic function can alter drug metabolism and result in toxicity.

Aggression occurs in approximately 25% of moderate-to-severe cases of Alzheimer’s disease

Patient assessment. In the case of acute-onset agitation, elicit a careful history from a caregiver or reliable informant. Patients should receive a complete physical and be assessed for signs and symptoms of medical illness, substance abuse, and falls.

Review all medications, and be on the alert for possible drug-drug interactions, particularly in patients recently

started on a new agent. Lab work should include electrolytes, hepatic and renal function tests (including BUN and creatinine), and a complete blood count to rule out infection or anemia. A BUN ratio above the normal range of 12:1 suggests the possibility of poor hydration.

Behavior assessment

After a physical cause of agitation has been ruled out, assess the scope, intensity, and frequency of the agitation symptoms and identify precipitating factors (eg, bathing, dressing, the unwanted presence of certain individuals). Environmental and social factors (table 2) can trigger behavior disturbances and also should be considered.

It also is important to determine:

- the duration, frequency, and severity of symptoms
- the pattern of the disturbance (eg, time of day an episode occurs)
- and which activities and caregivers typically precipitate agitation episodes.

Obtaining this information will help to monitor patient status and assess the efficacy of interventions. Caregivers can help by maintaining a caregiving diary that documents the information listed above. For a comprehensive patient-management approach, consult the McGraw-Hill Healthcare expert consensus guidelines for treatment of agitation in older persons, which can be downloaded from www.psychguides.com.

Spectrum of behavior symptoms

As noted, behavioral disturbances are characterized by a spectrum of initially unpredictable moods and conducts. Such deportment may manifest as disruptions, physically dangerous acts, psychological symptoms, and psychotic symptoms.⁷ Among the behaviors and symptoms commonly seen are delusions, disturbance of activity, aggression, sleep problems, and anxiety.

Psychotic symptoms. Delusions and hallucinations often occur in moderate stage dementia.⁸ Prevalence of psychotic symptoms in persons with dementia is approximately 19% for delusions and 14% for hallucinations.

Paranoid delusions are the most common type and account for approximately 40% of all delusions. The paranoid patient with dementia may be suspicious of a spouse or caregiver or believe that unknown perpetrators are hiding or stealing personal belongings.

Approximately 25% of patients with delusions are suspicious about the nature of their domicile (eg, believe they are in a residence other than their own). It also is common for patients to believe that a deceased relative is alive or that they continue to be employed when they are not.

Delusions and hallucinations must be differentiated from misremembering and misperceptions. For example, a patient may report a conversation or event that has “just happened” but that in fact occurred many years ago or may see a person on television and think that it is a friend or relative or that the person is actually in the room.

Disturbance of activity. Disturbance of activity is characterized by purposeless tasks such as packing clothes or household items for no reason, folding and unfolding clothes, removing items from drawers, pacing, and wandering. These symptoms usually worsen with dementia severity.

Aggression. Aggressive behavior is common among patients with dementia and occurs in approximately 25% of moderate-to-severe AD cases. Aggres-

sion is characterized by resistance to care, verbal outbursts, and physical combativeness. Aggression may be caused by frustration stemming from loss of the ability to perform certain tasks or engage in various activities, or the inability to understand the purpose of an activity. Thus, a patient may become upset when asked to bathe or change clothes. Caregiver frustration can also feed patient aggression.

Sleep disturbance. Fragmented sleep and frequent awakenings are common among patients with dementia. Daytime napping also is common. Nighttime sleep disturbances, especially when associated with wandering and agitation, can cause significant stress for caregivers. Such behavior can lead to nursing home placement.

Affective and anxiety disturbances. Major depression occurs most commonly in the earlier stages of dementia. Clinically, depression must be differentiated from apathy. Patients with dementia frequently have little interest in activities, and this may be misinterpreted as depression.

Sadness, tearfulness, suicidality, feelings of worthlessness, and melancholia are distinguishing signs of depression. Anxiety also is common, and may manifest as preoccupation with real or imagined upcoming commitments or appointments. Such preoccupations are common in mild dementia (approximately 40% of cases) but also are seen in moderate dementia. Fear of being alone and increased dependence on the caregiver also increase as dementia progresses.

Nonpharmacologic intervention

Clinical trials have shown that behavior interventions can reduce caregiver burden and delay patient institutionalization.⁹ Several behavior interventions may help address some of the agitated behaviors in dementia.

Activity planning. Daytime interventions include exercise, socialization, and recreation. A predictable routine may help minimize the risk of behavior episodes. One option is a day-care center special-

Table 2 Common triggers of behavior disturbances in persons with dementia

- Inability to channel energies constructively
- Anger and/or fear about the disease
- Frustration at not being able to complete tasks
- Anxiety about being bathed, dressed, toileted
- Response to institutional restraints
- Response to caregiver's anger, frustration, or fear
- Response to recent stressor (eg, death of a loved one)
- Noise; change in routine; lack of structure throughout day
- Overstimulation, understimulation
- New surroundings

Source: Prepared for Geriatrics by Judith Neugroschl, MD

izing in dementia. These centers provide structured activities and socialization, which allow for a safe outlet for patients and respite for caregivers. Patients or caregivers can contact local chapters of the Alzheimer's Association, churches, or nursing homes to obtain information about day care programs for persons with dementia.

Agitation that prevents a patient from functioning day-to-day warrants pharmacotherapy

ABCs. The mnemonic "ABC" is a reminder for patient assessment and refers to the Antecedents to disturbing behavior, the nature of the Behavior, and the Consequences of behavior. Once the ABCs have been clearly mapped out—for example by using information from a caregiver diary—it is possible to intervene to circumvent the behavior.

Ensuring safety. At any stage of dementia, bathroom railings, hand-held shower heads, and bath seats can help decrease the potential for conflict in the bathroom. Patients who spend significant time in a bed must be on a turning (repositioning) schedule to help

minimize the risk of ulceration, which can precipitate or exacerbate agitation. Although challenging to maintain, bathing and toileting schedules also are key to effective patient management.

Environment. Ensuring that a patient's surroundings are familiar and comforting can help reduce confusion or anxiety that precipitate behavior episodes. Clocks and calendars help patients with orientation to time. Patients with physical or sensory limitations should have appropriate assistive devices, such as glasses, dentures, and hearing aides. Hospital or nursing home rooms should be outfitted with familiar items.

Autonomy and freedom. Restraints may cause or exacerbate agitation, confusion, and distress; they are needed only in rare instances. An alternative is to give the patient access to a supervised setting in which freedom of movement (eg, walking, wandering) can occur safely.

Pharmacologic intervention

Pharmacologic intervention is indicated only if the behavioral disturbance prevents the patient from functioning or creates significant distress or danger. In general, if the symptoms are not severe, behavioral interventions should be tried first so as to avoid introducing medications that may cause increased morbidity. Keep in mind that just as antiarrhythmics may cause arrhythmias, antiagitation medications may worsen behavior symptoms.

continued

Table 3 Pharmacotherapy for behavior disturbances in dementia*

Agent	Starting dose	Total dose/d	Precautions
Antipsychotic			
Haloperidol (Haldol)	0.5 mg qd	1 to 3 mg	Serious: NMS Common: EPS, akathisia, TD, acute dystonia
Risperidone (Risperdal)	0.25 mg qd or bid	1 to 3 mg	Serious: NMS Common: sedation, EPS (less common than with haloperidol), hypotension, TD, hyperglycemia
Olanzapine (Zyprexa)	2.5 mg qhs or bid	5 to 10 mg	Same as risperidone
Antidepressant			
Trazodone HCl (Desyrel)	25 to 50 mg qhs or bid	50 to 250 mg	Hypotension, sedation, priapism (rare)
Anticonvulsant			
Carbamazepine (Tegretol, Eptol)	200 mg qhs	300 to 400 mg	Serious: Agranulocytosis, aplastic anemia, hepatitis, thrombocytopenia, Stevens Johnson syndrome Common: Sedation, unsteadiness
Valproic acid (Depakote, Depakene)	125 mg qhs	250 to 1,000 mg	Serious: Hepatic failure, pancreatitis, bone marrow suppression, thrombocytopenia Common: Nausea, sedation, tremor, hair loss, ataxia
Gabapentin (Neurontin)	100 mg qd or bid	300 to 2,400 mg	Serious: Leukopenia Common: Sedation, ataxia, tremor

*Supporting literature for these recommendations can be found in references 9-11,14-17

NMS: Neuroleptic malignant syndrome is a rare, potentially life-threatening idiosyncratic reaction characterized by severe rigidity, hyperthermia, confusion, markedly elevated creatinine phosphokinase, and unstable vital signs

EPS: Extrapyramidal symptoms; includes bradykinesia, tremors, and rigidity

TD: Tardive dyskinesia

Source: Prepared for Geriatrics by Judith Neugroschl, MD

For all agents, start with a low dose and use gradual and incremental dose increases; always monitor for side effects. Table 3 summarizes the dosing recommendations for management of behavior disturbances in patients with dementia. In general, attempts to reduce and eventually stop medications should be made after about 2 to 3 months, and, if that fails, intermittently thereafter.

In one of the most recent randomized, placebo-controlled trials testing pharmacologic management of agitation, findings showed no significant differences among the effects produced by haloperidol (Haldol), trazodone HCl (Desyrel), and behavior management therapy in 149 outpatients (mean age, 75). The medication groups exhibited a higher rate of adverse events (bradykinesia and parkinsonian gait) than the

behavior therapy and placebo groups, but no other significant difference in adverse events were seen.¹⁰ These results underscore the fluctuating nature of agitation and the need for more large-scale trials that more effectively answer questions about pharmacologic management of specific agitation symptoms.

Antipsychotic medications. Several large placebo-controlled clinical trials examining the role of antipsychotics in managing AD-related psychosis and disruptive behaviors demonstrated the effectiveness of haloperidol, risperidone (Risperdal), and olanzapine (Zyprexa).¹¹⁻¹³ Katz et al demonstrated the effectiveness of risperidone in managing aggression and psychosis.¹⁴ Haloperidol is associated with a higher rate of extrapyramidal symptoms than risperidone.

In general, atypical antipsychotics are considered first-line because of their side effect profile. The most common concerns with antipsychotics include parkinsonian symptoms, orthostatic hypotension, sedation, and tardive dyskinesia, a potentially irreversible movement disorder.

Antidepressants. Trazodone is a heterocyclic antidepressant with preferential serotonin reuptake inhibition. Case reports and open-label studies support its use for management of behavior disturbances in persons with AD. One very small double-blind study found that trazodone and haloperidol are equivalent in efficacy.¹⁵ Trazodone can also induce moderate sedation and therefore can be used to help manage sleep disturbance.

Patients with depression complicat-

ing their dementia can be treated with antidepressants. All antidepressants are similar in efficacy, but the selective serotonin reuptake inhibitors may be better tolerated than tricyclics.^{16,17}

Mood stabilizers. Carbamazepine (Tegretol, Eptol), valproic acid (Depakote, Depakene), and gabapentin (Neurontin) have all been evaluated for treatment of agitation. Most of the literature consists of open-label trial results, retrospective chart reviews, and case reports. In a placebo-controlled trial that enrolled 225 patients, carbamazepine, 300 mg/d (median dose), decreased aggression and produced significant global improvement.¹⁸ A placebo-controlled trial assessing the efficacy, tolerability, and safety of divalproex sodium (Depakote) showed that 375 to 1,375 mg/d can improve agitation symptoms associated with dementia. The most frequent side effects with divalproex sodium were sedation and GI disturbance.¹⁹ For carbamazepine and valproic acid, serum levels, CBC and hepatic function should be monitored. Drug-induced pancreatitis also is a possibility.

Hospitalization


Hospitalization for agitation should be considered if:

- the behavior disturbance is so severe that the safety of the patient or caregiver is compromised
- no reliable informant is available to observe and report on the patient's progress
- drug side effects preclude dosing adjustments on an outpatient basis.

Referral to a specialist—usually a geriatric psychiatrist—is recommended if the patient fails two or more trials of medication or if the primary care physician does not feel comfortable managing the side effects of the medications.

Conclusion

Behavior disturbances are common among persons with dementia. After ruling out physical factors and identifying the most likely cause of a disturbance, physicians should create a management plan that incorporates behavioral and pharmacotherapeutic

strategies. Encouraging caregivers and patients to maintain daily routines and minimize exposure to known triggers are important behavior strategies. Pharmacotherapy should begin only after careful observation of the patient and consideration of potential adverse effects of a particular drug. Drug types commonly used in the management of dementia-related behavior disturbances include antipsychotics, antidepressants, and mood stabilizers. 



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Turn to page 40 to take the exam

Detach or photocopy this page, place an X in the boxes that correspond to your answers, fill in your name and address, and mail (see address below). Answers must be received by October 1, 2002. A score of at least 80% must be earned to receive CME credit.

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1. Pharmacologic intervention for agitation is indicated only if the behavioral disturbance:
 - a. has a corresponding Medicare reimbursement code
 - b. has been documented by a caregiver and family member
 - c. accompanies dementia symptoms
 - d. prevents the patient from functioning or creates significant distress or danger
2. Which of the following can aid the daytime management of agitation:
 - a. structured activities and socialization
 - b. maintaining bathing and toileting schedules
 - c. enrolling a patient in an adult day care program
 - d. all of the above
3. Restraints should be used:
 - a. when a patient is confused
 - b. if a patient yells at a caregiver
 - c. rarely
 - d. when a patient criticizes managed care
4. Sadness, tearfulness, suicidality, feelings of worthlessness, and melancholia are distinguishing signs of:
 - a. depression
 - b. under dosing of antidepressants
 - c. resistance to care
 - d. tardive dyskinesia
5. Delirium, pain syndromes, infection, bladder distention, and fecal impaction can cause agitation, exacerbate it, or lead to dementia-related agitation.
 - a. True b. False
6. For pharmacologic management of agitation, attempts to reduce and eventually stop medications should be made after approximately:
 - a. 1 to 2 months
 - b. 2 to 3 months
 - c. 4 to 5 months
 - d. 6 to 7 months
7. In assessing a patient who displays agitation, it is important to determine:
 - a. the duration, frequency, and severity of symptoms
 - b. the pattern of the disturbance (eg, time of day an episode occurs)
 - c. the caregiver's understanding of drug-drug interactions
 - d. a and b
8. In the work-up of the patient who exhibits agitation, the first step is to:
 - a. schedule a psychiatric consult
 - b. rule out a physical cause
 - c. schedule an MRI
 - d. assess the patient's finances

In addition to the exam questions, answer the following evaluation questions: (1=strongly agree, 6=strongly disagree)

- | | |
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