

Aggression and Agitation in Dementia

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UNLABELED USE OF PRODUCTS/INVESTIGATIONAL USE DISCLOSURE:

Drs Wolf, Goldberg, and Freedman discuss the unlabeled/investigational use of medications for the treatment of aggression and agitation in dementia, none of which are approved by the US Food and Drug Administration.

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ABSTRACT

PURPOSE OF REVIEW: This article reviews the treatment of aggression and agitation in dementia. Both nonpharmacologic and pharmacologic approaches to responsive behaviors are discussed. Practical treatment strategies are applied to common behavioral symptoms.

RECENT FINDINGS: Aggressive and agitated behavior is common in dementia. Behavioral symptoms lead to reduced quality of life and distress for both patients and caregivers. They can also lead to poor outcomes and are associated with significant financial implications for the individual and health care system. A wide range of difficult behaviors exists, with limited evidence for deciding on treatment. Clinicians should integrate the available evidence with practical and commonsense strategies to target these difficult-to-treat behaviors.

SUMMARY: Treating aggression and agitation in dementia is challenging. Viewing behaviors as a response to either internal or external stimuli can help guide treatment. Treatment should emphasize nonpharmacologic approaches as an initial step, using practical and commonsense strategies. Caregivers and family should be actively involved in the planning and implementation of behavioral plans. It is essential to minimize both medical and nonmedical factors that may be contributing to behaviors. When pharmacologic options are required, it is important to choose medications that will target specific behavioral goals, having both practical consideration and the best evidence in mind.

INTRODUCTION

Behavioral symptoms are common in dementia and are a source of significant concern to all involved.^{1,2} Poor management of behavioral symptoms leads to reduced quality of life for the patient with dementia, increased distress in the caregiver, and, in some cases, distress in the clinician.³⁻⁶ Difficult behaviors can pose barriers to providing necessary medical investigation and treatment for patients. These behaviors can accelerate disease progression and functional decline, leading to greater utilization of health care services and prolonged inpatient stays in long-term care facilities or hospitals.¹ This has significant financial implications at personal, institutional, and government levels.^{4,5,7} Thus, neurologists and other physicians have a vested interest in effectively treating the behavioral

KEY POINTS

- To develop an effective intervention, it is important to view difficult behaviors as a response to a stimulus in the patient's internal or external environment.
- Before treating responsive behavior, it is important to accurately define and describe the nature and magnitude of the problem.
- Obtaining collateral information from multiple sources who are involved with the patient will give a richer and more accurate history.

symptoms of dementia, drawing on both nonpharmacologic and pharmacologic approaches.

UNDERSTANDING BEHAVIORS IN DEMENTIA

It is helpful to view aggressive and agitated behavior as *responsive behavior* that manifests in response to a stimulus in the patient's internal or external environment.⁸⁻¹⁰ These behaviors can represent the patient's attempt to communicate an unmet need to the caregiver, such as the experience of physical pain, hunger, loneliness, or boredom. Responsive behaviors can also occur in reaction to a stimulus perceived as stressful because of the patient's increased vulnerability to stress and reduced coping skills. Examples include noise, temperature, and relationship distress. Disruptive behaviors can be learned through modeling or reinforcement. For example, if a patient receives attention in response to a problem behavior (eg, screaming), the reaction of others (ie, attention) may unintentionally serve to increase the likelihood of the behavior recurring in the future.³ Preexisting personality factors, life experiences, current medical status, and history of trauma can also contribute to behavioral presentations.¹ Considering potential causes of responsive behavior will facilitate the development of appropriately targeted interventions.

Reviewing the patient's medical status is important for understanding triggers for responsive behavior. For example, an abrupt change in behavior can signal the development of delirium. Pain and discomfort can also trigger behaviors (**CASE 6-1**).^{8,11} It is important to note that a patient with dementia who has pain may not report discomfort because of significant cognitive impairment that prevents effective communication.

In addition, some medications, such as antipsychotics and serotonergic agents, can cause akathisia or restlessness. These signs may occur at high doses or if patients have significant sensitivity to these drugs. In addition, dopaminergic medications that are often used in Parkinson disease can result in psychosis. Finally, drug interactions and impaired renal or hepatic function can lead to higher effective doses than planned and thus may result in the emergence of signs and symptoms of agitation and aggression.

ASSESSMENT OF BEHAVIOR

The first step in treating responsive behavior is to properly define and assess the specific behaviors being reported.⁶ *Agitated behavior* is defined as "socially inappropriate verbal, vocal, or motor activity that is not a necessary by-product of a medical condition."¹² *Agitation* is a term used to describe a constellation of symptoms, including pacing, aimless wandering, performing repetitious mannerisms, and general restlessness. *Aggression*, categorized by both verbal and physical behavior, includes hitting, kicking, pushing, throwing or tearing things, spitting, biting, scratching, destroying property, grabbing people, grabbing objects away from people, hurting oneself or others, making sexual advances, cursing, and screaming.³

Although a patient may be described as "aggressive" or "agitated," it is important to obtain specific examples to determine if consensus exists about what has been witnessed. Obtaining a thorough understanding of the problematic behavior may take time, but it will ultimately save hours of frustration for all those involved by directing management down the correct course. Assessment of the behavior should include information about frequency, duration, whom it

affects, potential triggers, reinforcements of the behavior, and severity (ie, how significant or disruptive the consequences of the behavior are and whether it is manageable or not). The occurrence of responsive behaviors may have an identifiable pattern, such as occurring at a specific time of day, after a particular activity, or with a specific person. This information is important for identifying possible triggers that can be modified. The physician should also assess the degree of risk posed to the patient and others by the specific behavior. While all behaviors can be unpleasant, not all of them are dangerous. For example, hoarding does not put anyone at immediate risk, whereas pushing does. The physician should act quickly and effectively to address any behavior that puts the patient, another patient, staff, or a family member in harm's way. A thorough assessment of the situation will facilitate proper identification of the behavior and degree of risk, which will then dictate the course of action.

Information can be gathered in several ways as part of a thorough behavioral assessment. A primary source of information will be family members and close friends who have known the patient for a long time (ideally before the onset of the disease), who not only can identify current symptoms but can comment on the progression of symptoms over time. Family members are particularly essential to the assessment process when a patient is still living at home. When

An 86-year-old man was admitted to the hospital upon transfer from his long-term care facility for symptoms of verbal and physical aggression and agitation. He had been diagnosed with Alzheimer disease 4 years before the referral. His medical history included hypertension, benign prostatic hypertrophy with an indwelling catheter, and recurrent urinary tract infections. His family history was notable for Alzheimer disease in one of his siblings. He had a 2-year history of behavioral symptoms. On the day of transfer, he had physically attacked nursing home staff and was taken to the hospital by police.

CASE 6-1

On admission, he had an indwelling Foley catheter. Since he did not allow the Foley catheter to drain into a bag, it drained directly into an incontinence brief. He was confused, disoriented, and resistive to care. He was unpredictably aggressive and agitated. Following initial assessment, nursing staff identified a single behavioral trigger, which was the wetness he felt on his skin when the incontinence brief was soiled with urine. Since the patient refused to use a drainage bag, nursing staff decided to cap the catheter to prevent flow and emptied it every 2 hours. This creative solution kept the patient dry and eliminated all disruptive behaviors. No medication changes were made, and the patient was ready for discharge back to long-term care within a matter of days.

This case illustrates how pain or discomfort can trigger and maintain aggressive and agitated behaviors. It also demonstrates the need to think creatively to resolve behavioral disturbances and that an intervention does not have to be complicated to make a significant impact on symptom reduction.

COMMENT

attempting to get an accurate history from family members, it is important to ask questions, such as:

- ◆ What was the first thing you noticed that caused you concern? When was this?
- ◆ Why have you brought the person in now?
- ◆ Is this a change from how the person used to be? How so?
- ◆ When did you first notice this behavior?
- ◆ Has it gotten worse lately?
- ◆ What do you notice that makes this behavior worse or better?
- ◆ What have you tried in the past and has it helped?

Family members may not be able to answer all these questions with certainty, but if they are approached as experts on their loved one and treated as integral to patient care, they will typically provide a wealth of useful information. At times, responses can be verbose, potentially because of the family member's frustration with the disease or emotional state, and a physician must understand how to move an interview along in a respectful manner.

The health care team is another source of information about patient behavior. Whether the patient is in a long-term care facility or an acute hospital unit, nursing staff who have observed behaviors can report on them knowledgeably. It is important to consider input from nurses across all shifts, as patient behaviors can vary depending on the time of day and environmental factors. Many facilities use assessment tools to measure and track behavior over time (eg, the Agitated Behavior Mapping Instrument,¹² the Cohen-Mansfield Agitation Inventory,¹³ the ABC [Antecedent, Behavior, Consequence] Charting Approach¹⁴). These tools look at the antecedents, specific details, and consequences of a given behavior and may also take into account factors such as physical and emotional health, intellectual ability, environment, congruence between remaining capabilities and assigned tasks, and sociocultural background that may be contributing to the exhibited behavior.¹⁵ Therefore, in addition to the types of questions asked of family members, nursing staff should be asked to describe behavior, report on behavioral triggers and ameliorators, and highlight factors contributing to the presentation of behavior.

Obtaining a good understanding of the behaviors at baseline will optimize behavior management over the course of treatment. Establishing the rhythm of a patient's day can inform when a nonpharmacologic or pharmacologic intervention will be most helpful. If informants report that aggression is worse before care provision, the physician may decide that medication should be administered just before care. If informants report that a patient is particularly agitated just after lunch, routine behavioral intervention after lunch may be recommended, such as going for a walk or engaging in a music session. Over time, exhibited behaviors can be compared to baseline to determine the effectiveness of both nonpharmacologic and pharmacologic interventions and help shape next steps. Overall, available resources should be maximized when conducting behavioral assessments that serve as the foundation of effective intervention.

NONPHARMACOLOGIC INTERVENTIONS

Many nonpharmacologic approaches to intervention are effective not only in managing behavioral signs and symptoms but often also in targeting the

underlying causes of the behavior without the adverse side effects or possible drug interactions of medications.^{16–18} Nonpharmacologic interventions should be tried before contemplating pharmacologic interventions unless an acute risk of harm exists.^{3,8} If acute safety concerns are identified, aggressive treatment, including both nonpharmacologic and pharmacologic strategies, should be initiated quickly.

Nonpharmacologic approaches need not be complicated but do require some creativity (**CASE 6-1**). Often, choosing a small change in approach or introducing a thoughtful intervention may be enough to make a significant difference. One study demonstrated effective treatment of vocally disruptive behavior in a patient with frontotemporal dementia by simply giving the patient a lollipop.¹⁹ **TABLE 6-1**^{20,21} provides a summary of some of the most common nonpharmacologic strategies used in responsive behavior management.³ These strategies may be adapted to target a specific situation.

Several factors should be considered in selecting appropriate behavioral interventions, including the type of behavior and its associated degree of risk, the resources available to implement the strategy, the patient's personal preference and level of motivation, the patient's premorbid status (hobbies, interests, educational and occupational background, trauma history), the patient's current capabilities and strengths, and any medical barriers to engagement in certain activities. For example, unsupervised walking should not be recommended for a patient with unsteady gait who is at risk of falls, and physical exercise should only be considered if appropriately trained staff or family members are available to assist. Pet therapy should not be recommended if a patient is afraid of animals, and word games should only be recommended for a patient with minimal cognitive impairment. Appropriate interventions must be selected on an individualized basis, taking into account a host of factors, including intellectual capacity, physical and mental health, sociocultural background, and premorbid personality factors, to meaningfully address targeted behaviors in a patient-centered way.^{8,16,22,23} Here again, the input of family, friends, and the interprofessional care team is key in providing the physician with sufficient understanding of the patient's clinical presentation to facilitate the selection of appropriate interventions.

After strategies are identified as being potentially useful for a given patient, the physician should capitalize on the strengths of the individuals involved in the patient's care by delegating implementation of these interventions to family members, caregivers, and other members of the health care team (eg, psychologist, physical therapist, occupational therapist, recreational therapist, music therapist, dietitian, speech language pathologist, nurse). Team engagement is greatest when the instructions to delegates are respectful, specific, and concise and include the desired frequency, setting, time of day, location of supplies, and any other elements needed for the selected behavioral intervention. Because every patient is different and how the patient will respond to a given strategy is unknown, ongoing monitoring of the intervention's effectiveness is imperative. Thus, the physician should engage in behavioral assessment of the patient often during treatment. Once again, the physician may rely on assessment tools (as mentioned earlier in this article) and input from others (eg, family, interprofessional health care team) to ascertain if targeted behaviors have changed following the implementation of specific interventions. Looking at one or two time points is insufficient to make this determination, and the

KEY POINTS

- Using formal assessment tools to measure and track behavior can inform behavior management.
- Whenever possible, nonpharmacologic interventions should be tried before pharmacologic interventions.
- Using some creativity can allow for simple, but effective, nonpharmacologic interventions.
- Nonpharmacologic interventions should be tailored to suit the patient, caregivers, and environment.

physician should examine the overall net outcome over a predetermined length of time, typically 1 week, to determine if a behavior has improved.

PHARMACOLOGIC INTERVENTIONS

Limited evidence exists when it comes to deciding which medication to use for many behavioral symptoms. It is important to be familiar with the available evidence, but because medications are often ineffective in treating responsive behaviors, it may be necessary to improvise when evidence is lacking. It is often

TABLE 6-1 Common Nonpharmacologic Intervention Strategies for Managing Behavioral Symptoms of Dementia

General Strategy	Specific Examples
Physical activity	Structured exercise program (group or individual setting), walking indoors around the unit or hallways, walking outdoors
Sensory enhancement	For stimulation: music, sound-amplification devices, corrective eyeglasses, light therapy, ^a multisensory stimulation ^a
	For relaxation: music, massage, touch, white noise, noise-canceling headphones or earplugs, aromatherapy, ^a sleep therapy, quiet room
Social interaction	With people: live visits from family, friends, or elder clowns, one-on-one conversations with health care staff, simulated presence therapy (audio or video recordings of family or friends played to the person with dementia) ^a
	With pets: live pet visits, pet therapy, robotic pet interaction ²¹
Purposeful engagement	Activities that are meaningful and relevant to patients based on their current capabilities and previous interests, including games (ball toss, cards, jigsaw puzzles, crossword puzzles), music (attending concerts, singing, listening to the radio, music therapy), arts and crafts (painting, needlepoint, coloring, drawing, beadwork), technology (playing games on tablet, watching favorite sports games, watching a movie or TV show), and social interaction (see above)
Environmental design	Designated areas for wandering/pacing, group activities, and eating; using an established “quiet room” for behavior de-escalation; strategically preparing all designated spaces by painting appropriate murals to elicit the desired mood and patient response; using appropriate aesthetic materials (eg, avoiding multitoneal flooring); using appropriate labeling for patient rooms, bathrooms, and common areas and personal items; removing all unnecessary clutter from rooms
Differential reinforcement	Reinforcing desired behavior with rewards ⁶ ; using a token economy; modeling desired behavior
Staff/caregiver education	Training in building empathy for patients; using a gentle persuasive approach with patients; proper documentation of observed behaviors; psychoeducation regarding disease symptoms and progression; appropriate responses to delusional thoughts; self-care; stress management and coping strategies

^a The evidence for these particular interventions is mixed.^{1,20}

useful to borrow pharmacologic strategies from other conditions, such as mood disorders, anxiety disorders, obsessive-compulsive disorder, and traumatic brain injury, when similarities exist between these conditions and the responsive behavior. For example, a patient with repetitive, compulsivelike, disruptive behaviors may respond to medications for obsessive-compulsive disorder. Moreover, because symptoms are often difficult to treat, can present significant safety concerns, and may affect quality of life, considering evidence from case reports and open-label case series may be justified.

Using medications in patients with dementia requires consideration of a number of factors. Medication interactions can cause an increase or decrease in therapeutic levels of medication. This can lead to reduced effectiveness of some medications or increased adverse reactions. It is thus important to be aware of interactions of commonly used medications when choosing pharmacologic treatments and to closely monitor the effects of medications. Medication should be started at a small dose, especially in frail patients, usually about half of the typical starting dose for younger patients. **TABLE 6-2**²⁴⁻²⁷ lists the most common medications used to treat behavioral symptoms and common dosing strategies. If possible, dose increases should be slow and no more frequent than every 1 to 2 weeks, both to ameliorate possible side effects and to monitor for response and adverse reactions. Making one medication change at a time makes it easier to know which change is truly responsible for an improvement or worsening of behavior. It is reasonable to target a therapeutic dose, keeping in mind that effective doses vary significantly and that overshooting the effective dose can, at times, exacerbate symptoms. The maximum dose is often considerably lower than that used in younger patients. Often, the first medication trial will not be effective and switching to another agent will be needed. After a number of trials of monotherapy, it may be necessary to combine medications that have different mechanisms of action, especially if a patient shows partial response to one medication. Common side effects in patients with dementia include sedation, extrapyramidal signs, falls, hypotension, worsening of behavior, and emergence of new behavioral features.

It is important to decide which behavior to target with a pharmacologic option. When a patient has multiple problematic behaviors, the physician should prioritize which behavior to target first, considering the severity, distress, and concern for the patient's or others' safety. Some behaviors are easier to target and more likely to respond to pharmacologic intervention and may thus be prioritized. If multiple behaviors are problematic, hypothesizing whether they relate to one another can help guide which behavior to target first. For example, if a patient is restless and paranoid, it can be hypothesized that the paranoia may be driving the restlessness. In this case, the initial target would be the paranoia. Using a commonsense and individualized approach to pharmacologic treatment will help steer the physician to more effective treatment of difficult behaviors.

SPECIFIC BEHAVIORS

The following are some of the most common aggressive or agitated behaviors a physician encounters, with suggestions for how to treat them from nonpharmacologic and pharmacologic perspectives (**TABLE 6-3**). The strategies listed are not meant to be exhaustive; rather, they demonstrate an approach to common situations that can be easily implemented and modified based on the specifics of each case.

KEY POINTS

- Evaluating the outcome of nonpharmacologic interventions will help determine if they have been helpful or if modifications should be made.
- The pharmacologic approach to treating responsive behavior includes using the best evidence available but also improvising when evidence is lacking.
- It is important to titrate medications slowly and monitor for adverse effects or worsening of behavior.
- Deciding which behavior to target first requires prioritizing safety concerns and patient and caregiver distress as well as understanding the factors contributing to the behavior.

TABLE 6-2 Common Medications Used to Treat Behavioral Symptoms

Medication	Usual Starting Dose	Usual Maximum Dose
Antidepressants		
Citalopram	10 mg/d once daily	20 mg/d once daily ^a
Escitalopram	5 mg/d once daily	10–20 mg/d once daily ^a
Sertraline	25 mg/d once daily	150–200 mg/d once daily
Venlafaxine XR	37.5 mg/d once daily	150–225 mg/d once daily
Duloxetine	30 mg/d once daily	60 mg/d once daily
Clomipramine	10–25 mg/d once daily	200 mg/d split dosing
Doxepin	10 mg/d usually dosed at night	100 mg/d usually dosed at night
Trazodone	25 mg/d once daily	250 mg/d split dosing
Mirtazapine	7.5 mg/d usually dosed at night	45 mg/d usually dosed at night
Antipsychotics		
Risperidone	0.25 mg/d once daily	1–2 mg/d split dosing
Olanzapine	2.5 mg/d once daily	10–15 mg/d split dosing
Quetiapine	25 mg/d once daily	200 mg/d split dosing
Clozapine	6.25 mg/d usually dosed at night	50–100 mg/d split dosing
Cognitive enhancers		
Donepezil	5 mg/d once daily	10 mg/d once daily
Galantamine	8 mg/d split dosing	24 mg/d split dosing
Galantamine ER	8 mg/d once daily	24 mg/d once daily
Rivastigmine	3 mg/d split dosing (oral) 4.6 mg (24-hour transdermal patch)	12 mg/d split dosing (oral) 13.3 mg (24-hour transdermal patch)
Memantine	5 mg/d once daily	20 mg/d split dosing
Memantine ER	7 mg/d once daily	28 mg/d once daily
Anticonvulsants		
Gabapentin	100 mg/d once daily	900 mg/d split dosing
Carbamazepine	100 mg/d once daily	300 mg/d split dosing
Topiramate	25 mg/d once daily	100 mg/d split dosing
Lamotrigine	25 mg/d once daily ^b	200 mg/d split dosing
Hormonal treatments		
Cyproterone acetate	10 mg/d once daily	10 mg/d once daily
Leuprolide	7.5 mg/d IM every month	7.5 mg/d IM every month
Medroxyprogesterone	100 mg/d IM every 2 weeks	300 mg/d IM every 2 weeks

IM = intramuscular.

^a In those age 65 years of age and older, the maximum recommended dose of citalopram is 20 mg/d²⁴ and the maximum recommended dose of escitalopram is 10 mg/d²⁵ (Health Canada). The US Food and Drug Administration (FDA) recommends a maximum dose of 20 mg/d for citalopram in those older than age 60.²⁶ For escitalopram, the recommended dose is 10 mg/d in the elderly.²⁷

^b If drugs that inhibit metabolism of lamotrigine (such as valproic acid) are used, the starting dose is 25 mg every other day.

Physical and Verbal Disruptive Behaviors

Physical and verbal disruptive behaviors comprise one of the main safety concerns posed by responsive behaviors and represent the most common concerns of family members and health care staff. These include aggressive behaviors such as hitting, kicking, pushing, throwing or tearing things, spitting, biting, scratching, and destroying property. Nonaggressive physical behaviors include exit seeking and entering the rooms or personal space of others. Verbal aggressive behavior includes cursing, screaming, and making disruptive noises.

NONPHARMACOLOGIC APPROACH. Because of the pervasiveness of these behaviors, it is important to assess the frequency, degree of risk, and potential triggers. Keeping a log of when the behavior occurs, including antecedents and consequences, will help to establish patterns of occurrence and identify precipitating factors. This can also help target the most appropriate times for intervention, corresponding with the peaks of the behavioral display.

If environmental triggers are identified, patients can be removed from the triggering environment and kept away from what is perceived as stressful, such as noise and overstimulation. Providing earplugs or noise-canceling headphones can help reduce the noise and subsequent stress experienced by the patient. Additionally, the environment can be altered to meet the needs of the patient. Examples are introducing white noise or calming music and minimizing stimulating noise in the environment. Small changes in the environment can make a big difference if patients are exit seeking or entering other patients' rooms. For example, painting the exit door to look like a bookshelf, putting a stop sign on the door of someone's room, or covering the doorway with a sheet may deter a patient from attempting to go through those doorways. The sheet serves as a visual barrier blocking entrance to the room and thus need only be about 2 feet to 3 feet wide.

Disruptive behaviors can indicate physical or emotional discomfort. This is especially the case with restlessness; thus, it is important to look for subtle clues suggesting discomfort or pain. It is important to think broadly in terms of the causes of discomfort and pain that patients may experience; for example, rectal prolapse, hemorrhoids, and constipation should not be overlooked. In these situations, optimizing management of behavioral triggers is essential. As illustrated in **CASE 6-1**, a small change in routine service delivery can alleviate discomfort with significant effect and eliminate disruptive behaviors.

It is also important to assess for emotional distress, looking for features of anxiety and depression. Patients with significant cognitive impairment may not be able to verbalize that they are anxious or depressed. Depression should be considered if the patient is tearful or seems to be very negative, especially if the patient has withdrawn from activities and social interactions. Associated symptoms include lack of appetite and poor sleep. Anxiety can be identified by the appearance of being fearful, wringing of the hands, worried facial expression, continuous requests for help or reassurance, or repeated vocalizations (**CASE 6-2**). Premorbid history of depression, anxiety, or trauma can be an important clue to the possible presence of emotional distress.

When emotional distress is suspected, behavioral interventions should focus on creating a safe environment for the patient. Implementing appropriate recreational activities, especially if they can create positive experiences, may be

KEY POINTS

- If environmental factors are triggering behaviors, reducing the impact of the environment on the patient or modifying the environment may be helpful.
- Disruptive behavior can be an expression of either physical or emotional discomfort.

helpful for patients who are depressed. Patients who are anxious may benefit from being with calming people and being positioned close to the nursing station, where they may feel safer.

PHARMACOLOGIC APPROACH. Before initiating medications to treat disruptive behavior, it is important to explore if existing drugs are contributing to the behaviors. It is helpful to review recent medication changes and explore the possibility that these may have contributed to the emergence of symptoms. Dopaminergic medications, as well as cholinesterase inhibitors and stimulating antidepressants such as fluoxetine, may be activating and may thus contribute to agitation. Reducing or eliminating these medications should be the first step if they are felt to be contributing to disruptive behavior.

TABLE 6-3 Summary of Approach to Common Behaviors

Behavior	Nonpharmacologic Approach Options	Pharmacologic Approach Options
Physical and verbal disruptive behavior	<ul style="list-style-type: none"> Modify environment to be less stimulating or triggering Remove patient from overstimulating environment Treat potential physical discomfort Create an environment that is emotionally supportive 	<ul style="list-style-type: none"> Reduce or eliminate activating medications Avoid antipsychotic medications unless acute safety concerns exist or psychosis is driving behavior Use antidepressants if depression is thought to drive behavior Consider using other classes of medications, such as anticonvulsants or low-dose benzodiazepines, or memantine
Avoidance and resistive behavior	<ul style="list-style-type: none"> Try smaller and more frequent food portions if food is refused Simplify medication regimen to improve compliance Cautiously hide medication in food or drink if the medication cannot be detected Prioritize the type and frequency of care that is required Develop a gentle and soothing approach to care that is understood by the patient 	<ul style="list-style-type: none"> Reduce or eliminate medications that can decrease appetite Introduce medication that can stimulate appetite Trial a stimulant if apathy is thought to be a factor Treat psychosis or mood if these are thought to drive the behavior Use sedating or calming medications before care
Perseverative and repetitive behavior	<ul style="list-style-type: none"> Optimize treatment of physical or emotional discomfort Provide more acceptable sensory stimulation, including textured material and sound amplification devices Increase engagement in activities suited to the patient's abilities 	<ul style="list-style-type: none"> Treat obsessional qualities with serotonergic antidepressant medications Target vocalization behavior with doxepin

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Aggressive behaviors that put the patient or others at risk should be treated urgently. Since atypical antipsychotics such as risperidone, olanzapine, and quetiapine have the most evidence,²⁸ they should be considered as a treatment option and titrated up to a tolerated and effective dose, especially if psychotic symptoms are thought to drive the aggressive behaviors. However, these medications may cause extrapyramidal side effects that could impair gait and predispose the patient to falls. Thus, if the patient has parkinsonism or balance problems for other reasons, the authors suggest avoiding antipsychotics, if possible, and considering a trial of trazodone because of its rapid onset of action and sedative qualities. Moreover, if a patient has responsive behaviors without psychosis, the authors often give a trial of trazodone before prescribing an antipsychotic because of the better safety profile of trazodone, especially as related to risk of falls. Other commonly used options include memantine²⁹ because of

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Behavior	Nonpharmacologic Approach Options	Pharmacologic Approach Options
Disinhibition and hypersexuality	<ul style="list-style-type: none"> Provide appropriate outlets to show affection Allow patient privacy (alone or with spouse) Use differential reinforcement strategies 	<ul style="list-style-type: none"> Investigate pain or discomfort in genital areas Reduce or eliminate dopaminergic medications and benzodiazepines Trial serotonergic antidepressant medications or hormonal treatments
Hyperoral behavior	<ul style="list-style-type: none"> Assess nutritional intake Remove or secure objects that are dangerous if ingested Remove patient from dining room when food is served Use cues to distinguish nonfood from food items Substitute unhealthy foods with healthy choices or other forms of oral stimulation 	<ul style="list-style-type: none"> Reduce or eliminate medications that stimulate appetite Trial serotonergic antidepressants, stimulants, or topiramate
Hallucinations and delusions	<ul style="list-style-type: none"> Provide support and education to caregivers if symptoms are not harmful or distressing to patient Optimize visual and auditory senses or enhance sensory stimulation Do not argue with patient about delusional beliefs Explore whether symptoms are an expression of underlying feelings or attitudes 	<ul style="list-style-type: none"> Reduce or eliminate dopaminergic medications Consider a cautious trial of antipsychotic medication Trial a cholinesterase inhibitor if indicated Trial an antidepressant medication if anxiety or depression is present

CASE 6-2

A 71-year-old non-English-speaking man was admitted to the hospital for treatment of aggression, restlessness, sleep disturbance, and exit seeking in the context of a 3-year history of cognitive impairment. Other symptoms included incoherent speech, hallucinations, and delusions. His medical history was positive for depression, anxiety, and mild hearing loss. The differential diagnosis included dementia with Lewy bodies and Alzheimer disease.

During admission, the patient's anxiety presented as constant religious chanting, worried facial expression, and rapid breathing. The patient talked to himself in the mirror, voided urine inappropriately overnight, was resistive to care (including being toileted and changed into clean clothes), and was physically aggressive toward other patients and staff. Interdisciplinary team discussion and consultation with family members yielded the identification of several behavioral triggers, including fear and shame of being disrobed, fear of personal items being stolen from him, and fear of being assaulted by other agitated patients. Several nonpharmacologic interventions were implemented. A pocket talker (a sound amplification device equipped with a headset and microphone, often worn around the neck or clipped to an individual's clothing) was introduced to target sensory deprivation due to hearing loss. Staff ensured that his genital area was covered during care and did not provide liquids after 8 PM. His mirror was covered. He was taken for a walk during shift changes and offered headphones playing audio versions of his religious texts to calm him when anxious or restless.

The pharmacologic approach first focused on targeting his restlessness. Antipsychotics were initially avoided because he had mild parkinsonism, and dementia with Lewy bodies was in the differential, raising concerns about neuroleptic sensitivity. Trazodone was started at a small dose and slowly increased. As restlessness started improving, anxiety symptoms became more prominent and escitalopram was started. Escitalopram was not helpful, and he began to have difficulty sleeping at night, so it was stopped and mirtazapine was tried with good results. Although his anxiety and sleep improved, he had episodes of physical aggression that put other patients and staff at risk. At this point, quetiapine was cautiously added, and his aggressive behavior resolved.

COMMENT

This case highlights the importance of gaining family input, the contribution of cultural background, and the impact of sensory deprivation on symptom presentation. This case also demonstrates using a strategic pharmacologic approach that targets specific symptoms in isolation, using both evidence-based and practical considerations.

its potential calming effect and selective serotonin reuptake inhibitors (SSRIs) based on literature that citalopram may be beneficial for aggression.³⁰ Anticonvulsants, especially carbamazepine, may have some benefit. Limited evidence exists for the use of gabapentin, lamotrigine, and topiramate.³¹ Cautious use of benzodiazepines, such as lorazepam as a relatively short-acting drug, may be considered as well. If a long-acting benzodiazepine is needed, clonazepam may be considered.

If depression or anxiety are suspected, an SSRI, such as citalopram, escitalopram, or sertraline, is often used initially. If this is not helpful, a serotonin norepinephrine reuptake inhibitor (SNRI), such as duloxetine or venlafaxine, may be tried. If more immediate results are needed, trazodone can be used for its calming effect and sedative properties. Trazodone and mirtazapine may also be helpful if a patient has associated sleep disturbance. For anxiety, a benzodiazepine, such as lorazepam or clonazepam, in small doses may be helpful. Antipsychotics, particularly quetiapine, can be helpful for mood and anxiety symptoms, especially if a patient has associated psychotic symptoms.

Avoidance and Resistive Behavior

Patients who are resistant to taking their medication or eating food pose a common challenge.

NONPHARMACOLOGIC APPROACH. As for other behaviors, it is important to look for common causes, including pain, infection, or other medical contributors. Swallowing ability should also be assessed. Looking for indications of paranoia or depression can help uncover additional factors driving these behaviors. It is important to assess the nutritional requirements for patients refusing meals. At times, substituting meal supplements or introducing smaller food portions more frequently throughout the day may be an acceptable compromise that allows for adequate nutrition. Marginally beneficial medications can be reduced and stopped or the schedule of medication can be simplified to once or twice a day if possible. Observing when and with which activities the patient seems to be more compliant can aid in the selection of appropriate times to provide meals, snacks, and medications. Crushing or substituting rapidly dissolvable or liquid forms of medications or changing the texture of food may be helpful. Hiding medication in food or drink can be a good strategy as long as the patient is not able to detect the medication by vision, taste, or smell.

Refusal, avoidance, or physical and verbal aggression during provision of care is very common in patients with dementia. Occasionally, this is prompted by compromised intellectual capacity that limits the patient's understanding of why he or she is being disrobed or handled, leading to distress and subsequent resistive behavior. Helping the caregiver prioritize the type and frequency of care that is required can be helpful. It may be reasonable for the patient not to shower or shave daily, although this was the norm in the past. Educating family members about balancing the need to keep the patient calm and safe versus hygiene factors is important, as many family members have difficulty letting go of habitual routines. A certain level of hygiene is necessary, however, and once it is determined that care needs to be provided, the way care is delivered should be tailored to the patient's cognitive capacity. It is important to use a gentle persuasive approach and speak in a calm manner, using short sentences and simple commands to clearly explain what will be done

KEY POINTS

- It is important to reduce or eliminate medications that may be contributing to disruptive behavior.
- Avoidant and resistive behaviors can be driven by medical contributors such as pain, infection, and swallowing difficulties or by neuropsychiatric contributors such as depression and psychosis.
- Treating behaviors that prevent provision of personal care requires looking for compromises in nonessential tasks and providing education to family and caregivers.

before doing it. For patients whose verbal comprehension is compromised, using visual cues to communicate the caregiver's intentions in the form of pictures and gestures may be useful. Establishing a care routine so that the patient and family know what to expect can be assistive. Incorporating music and other calming environmental stimuli may also be helpful. Wherever possible, it is helpful to include the patient in care provision. For example, asking the patient to hold the washcloth or toothbrush may facilitate cooperation. Care can also be modified; for example, a sponge bath of the genital and perineal area may be provided as opposed to a full shower if the patient is highly agitated.

PHARMACOLOGIC APPROACH. Some medications can cause either stomach upset or reduced appetite, leading to refusal to eat. These include cholinesterase inhibitors and serotonergic medications. Reducing or eliminating these medications may be helpful.

Certain medications are known to stimulate appetite and can be used if patients refuse to eat and are losing weight. Antipsychotics, especially olanzapine, may increase appetite and cause weight gain. This is a particularly good option if some degree of psychotic symptoms is present. Mirtazapine also stimulates appetite and is an especially good option if depression or anxiety is present. Mirtazapine is also a sedating medication in low doses and can be used if sleep disturbance is present. However, in higher doses, mirtazapine can lose its sedating effect and become stimulating.³² The authors sometimes use meggestrol, which is used for chemotherapy-induced anorexia, to help stimulate appetite. If apathy is thought to be driving reduced appetite, a stimulant such as methylphenidate may be tried.³³

If paranoia or psychotic symptoms are suspected to be driving responsive behaviors, antipsychotics should be considered. Depressive and anxiety features that may be contributing to behavioral symptoms can be treated with antidepressants.

Behaviors during care are difficult to treat pharmacologically. A sedating or calming medication, such as lorazepam or trazodone, can be given before care with the hope that the medication will have some effect by the time care is administered. At times, it is sufficient to change the timing of sedating or calming medications to administration just before care provision. In patients who have evidence of other symptoms during the day, such as psychosis, mood, or agitation in general, targeting these symptoms may result in less agitation during care.

Perseverative and Repetitive Behavior

Perseverative and repetitive behaviors are common in dementia. Examples include repetitive banging, skin picking, asking questions, and calling out for help. These behaviors can be disruptive to caregivers, family members, staff, and other patients and can even be harmful to the patients themselves.

NONPHARMACOLOGIC APPROACH. These behaviors can be conceptualized as arising from a need to self-soothe or a lack of stimulation. A patient who is banging his or her head against the wall repetitively may be in some type of distress and trying to self-soothe and obtain comfort. Investigating physical sources of distress, such as pain or discomfort, is extremely important. Localizing the source of

discomfort can be challenging, although clues often exist. For example, repetitively picking skin on the hand and banging the hand against objects can indicate pain or discomfort in the hand. Emotional discomfort can be targeted by providing emotional support in the form of individual attention or conversation. Sensory deprivation can be approached by providing other, more appropriate, sources of sensory stimulation using several different senses. For example, patients can be provided with nonharmful textured objects to feel, such as carpet samples with different textures or piles. Some children's toys may also provide sensory stimulation if the patient is able to manipulate different components that are movable and can generate sounds. Sound amplification devices (such as pocket talkers or hearing aids) and corrective eyeglasses may also provide needed sensory input (**CASE 6-2**). Patients suspected of not having enough stimulating purposeful activity can be engaged in activities suited to them, such as playing a game (eg, cards), painting or drawing, and playing catch with a ball or balloon.

PHARMACOLOGIC APPROACH. The obsessional quality to these behaviors suggests that medications commonly used in obsessive-compulsive disorder may be helpful. These include SSRIs such as escitalopram and sertraline. Tricyclic antidepressants, such as clomipramine, are less well tolerated but can be helpful.³⁴ In vocalizations, doxepin has shown some indication of benefit.³⁵

Disinhibition and Hypersexuality

Disinhibition and hypersexual behaviors can be both distressing and harmful. Although these behaviors are typically linked with behavioral variant frontotemporal dementia (bvFTD),¹⁴ they can be found in other forms of dementia as well. Common examples include taking food from other people's plates, disrobing, exposing the genital area, masturbating, making physical or verbal sexual advances, and asking inappropriate personal questions of staff or other patients.

NONPHARMACOLOGIC APPROACH. These behaviors can, at times, be driven by the need for affection or physical or emotional intimacy. Ensuring that the patient experiences affection even in nonsexual ways is important. The need for affection through touch can be facilitated by providing a pet (live, toy, or robotic) for the patient to touch and stroke.

The sexual needs of patients with dementia are an important and often neglected topic. The patient's partner may struggle with understanding the physical and emotional changes in their relationship. It is important to be supportive and allow the patient and partner permission to have open discussions about these challenges and to help problem solve when needed. Couples often have difficulty with intimacy in institutional settings because of lack of privacy. Ensuring the availability of private time without interruption by staff or other patients is important.

Some situations can evoke ethical concerns or discomfort from family or staff. For example, a patient engaging another patient in sexual activity in an institutional setting brings up considerations of capacity and, at times, legal concerns. These concerns should be clarified and the family engaged to make decisions that are in the best interest of their loved one. Another example is disrobing or masturbating, which can elicit discomfort in staff or family. Family and staff often benefit from education about the nature of sexual needs and urges

KEY POINTS

- Perseverative and repetitive behaviors can be related to physical or emotional discomfort or to sensory deprivation.
- Disinhibited and hypersexual behaviors can be driven by need for affection and intimacy and mediated by difficulties with judgment.

in the patient with dementia to allay feelings of guilt or anger at the patient for acting on sexual urges. Allowing for behaviors that do not harm others in a safe and private environment can be a reasonable approach.

Some disinhibited sexual behaviors are not appropriate and need to be modified. Using behavioral techniques such as differential reinforcement to reward patients when they do not display sexual behavior can condition them to act more appropriately. For example, consider a patient who exposes his genitals to others. After carefully assessing the frequency of the behavior, it is determined that he exposes himself approximately every 20 minutes. Providing incentives or rewards for 20-minute periods when he has not exposed himself can reduce the reoccurrence of the genital exposure over time.

PHARMACOLOGIC APPROACH. It is important to look for medical contributors to disinhibited and sexual behavior. Pain or discomfort in the genital area can lead to behaviors involving the genitals, such as self-stimulation and exposing. Dopaminergic medications can also drive these behaviors, as can benzodiazepines, which can cause disinhibition. Reducing these medications and treating any pain triggers are important first steps in managing these behaviors.

A number of pharmacologic treatments exist for inappropriate sexual behavior.³⁶ Antidepressant medications may be used to capitalize on the common side effect of sexual dysfunction. They may also have antiobsessive properties that can be helpful. Common antidepressants used in these situations include trazodone, paroxetine, citalopram, and clomipramine. Some evidence exists for the use of quetiapine. Hormonal medications, such as cyproterone, medroxyprogesterone, and leuprolide, can also be helpful in patients with inappropriate sexual behavior.

Hyperoral Behavior

Hyperoral behavior is a key feature in bvFTD⁴⁴ but is also found in other dementia syndromes. A spectrum of problematic behaviors that involve eating and oral behavior exists. Increased food cravings and carbohydrate intake can lead to significant weight gain and metabolic disorders. Food-seeking behavior can lead to stealing or grabbing food from others, which can ultimately lead to interpersonal conflict and physical harm. Rapid eating of food or oral exploratory behavior can present an aspiration or asphyxiation risk. Eating nonedible objects can be dangerous, such as in the case of a patient who ate raw meat, telephone cords, rubber gloves, and feces.

NONPHARMACOLOGIC APPROACH. In trying to manage hyperoral behavior, it is helpful to involve a dietitian to assess nutritional intake to ensure that meals and appropriate nutrients are being consumed. Clearly maintaining a safe environment is important, and objects that are harmful and can be put in the mouth, including poisonous plants, should be secured or removed. At times, it may be helpful to remove the patient from a common dining room when food is present, such as during mealtimes when the patient may grab food from other patients. Visual perceptual difficulties or deficits in object recognition may lead the patient to identify some nonfood items as food. In these situations, using creative cues to allow the patient to distinguish nonfood from food items can be helpful, for example, teaching the patient that food items will only be presented to him or her on a red placemat and that anything not on the red placement is not

fit for consumption. Substituting less healthy foods with other foods that have fewer calories can also be attempted. The need for oral stimulation can be targeted by using a baby chew toy, wet washcloth, or chewing gum, if deemed safe.

PHARMACOLOGIC APPROACH. Before trying to treat hyperoral behavior pharmacologically, it is important to review the medications the patient is already taking. Some medications have a propensity to increase appetite and food intake, which may be driving the hyperoral behavior. Any of the atypical antipsychotics can do this, especially olanzapine and clozapine. Antidepressants also have this quality, especially mirtazapine. If feasible, these medications should be reduced or eliminated.

The anticonvulsant topiramate has some evidence for reducing weight gain related to antipsychotic medications³⁷ and binge eating disorders³⁸ and may play a role in treating hyperoral behavior in dementia.³⁹ Medications that target obsessional behaviors, such as SSRIs⁴⁰ and clomipramine,³⁴ can be tried. Stimulants may be helpful in treating binge eating disorder.⁴¹ Thus, trying a stimulant such as methylphenidate may be considered if other strategies are not helpful.

Hallucinations and Delusions

Psychotic symptoms are common in dementia and are the most strongly linked to poor outcome, long-term care placement, and caregiver stress.^{8,42} Although psychotic symptoms themselves may not be agitated or aggressive behaviors, they are commonly the driving factor for these behaviors. Psychotic symptoms are part of the diagnostic criteria for dementia with Lewy bodies (DLB) but are also common in other dementias, including Alzheimer disease, bvFTD, and vascular dementia.⁴³

NONPHARMACOLOGIC APPROACH. The most frequent perceptual abnormalities that result in behavioral difficulties are visual and auditory hallucinations.⁴³ Delusions are defined as “fixed beliefs that are not amenable to change in light of conflicting evidence.”⁴⁴ These can emerge in dementia and frequently lead to behavioral difficulties. Common delusional themes in patients with dementia include persecution (eg, someone is trying to steal from them or harm them in some way), grandiosity (eg, they are special or have special abilities), and infidelity (eg, spouse is being unfaithful).

Although psychotic symptoms often lead to behavioral difficulties, this is not always the case. For example, in DLB, it is quite common for the patient to have nondistressing or even pleasant visual hallucinations. The inability to recognize one’s reflection in the mirror, a form of delusional misidentification syndrome (also known as the *mirror sign delusion*), is common in DLB (**CASE 6-2**).⁴⁵ These examples highlight the fact that not every symptom requires treatment.⁶ The most helpful intervention when delusions do not require treatment is often providing education to the caregivers and family members about the nature of the disease and providing support to deal with these distressing symptoms.

Inadequate sensory stimulation resulting from poor vision or hearing can contribute to the emergence of hallucinations (**CASE 6-2**).⁸ Assessing a patient’s vision and hearing is therefore an important first step in determining the cause of hallucinations. Optimizing the visual and auditory senses by introducing assistive devices, such as a hearing aid, a pocket talker, or eyeglasses, can be helpful in

KEY POINTS

- When hyperoral behavior is present, it is essential to ensure that the environment is safe from objects that can be harmful if ingested.
- Psychotic symptoms that are not distressing or harmful to others do not need to be treated.

eliminating or reducing hallucinations. At times, it is helpful to consider enhancing sensory stimulation through other means, such as by brightening the lights, talking louder, or playing music. Stimulating other senses may be beneficial as well, such as by introducing aromatherapy or massage therapy.⁴⁶ In one case, a patient had a delusion in which he believed he heard people talking about him. The muffled sounds of people talking in the hallway outside of his room contributed to this delusion, which was resolved when a white noise machine was used to block out the noise from the hall.

Since delusions are fixed and firm beliefs, it is not wise to argue with the veracity of the delusion. Rather, agreeing or accepting the beliefs as the patient's reality is often more helpful. Caregivers and staff could, in some cases, play along with a delusion to reduce agitation or aggression. For example, a patient who believes that he or she is the chief executive officer of a company may benefit from being treated as if he or she is in the office, and, where appropriate, creating an office environment in the patient's room may be useful.

Delusions may be an expression of an underlying feeling or attitude. For example, in the case of a delusion regarding infidelity, the patient may be trying to communicate feelings of abandonment, loneliness, or estrangement from his or her spouse, which are not uncommon feelings in the disease process as relationships undergo many changes. Awareness of these possible feelings may facilitate management.

PHARMACOLOGIC APPROACH. When considering the use of medications to treat psychotic symptoms, first consider whether the patient's current medications can contribute to the psychotic symptoms being targeted. For example, dopaminergic medications, such as pramipexole or levodopa, are known to contribute to psychosis.⁴⁷ If medication effects are suspected, slowly reducing the dose or discontinuing the medication should be considered.

If nonpharmacologic strategies are not sufficient to manage the symptoms, antipsychotic medication may be warranted. It is important to be familiar with adverse effects of antipsychotic medications, including an elevated risk of cerebrovascular events. Antipsychotics also carry a black box warning from the US Food and Drug Administration (FDA) about an increased risk of mortality with their use in dementia.⁴⁸ Despite these risks, antipsychotics have the strongest evidence for efficacy²⁸ and are commonly used, especially if a patient is in significant distress or safety concerns are present. Typically, substitute decision makers will agree to these medications despite the risks when the rationale is explained clearly. Of the antipsychotic medications, risperidone has the advantage of being less sedating and less likely to cause orthostatic hypotension than other antipsychotics. However, it does have a higher risk of extrapyramidal symptoms than the other atypical antipsychotics. Olanzapine is a sedating atypical antipsychotic and commonly causes weight gain. These properties can be used in situations in which sedation is desired or if a patient refuses to eat and is losing weight. Quetiapine has a low risk of extrapyramidal symptoms and is useful when concern exists about extrapyramidal side effects such as in Parkinson disease or DLB. It may also have some mood-stabilizing properties. In patients with high sensitivity to extrapyramidal symptoms, clozapine should be considered and started in low doses.⁴⁹ Frequent blood work is required when using clozapine to monitor for agranulocytosis.

Some evidence exists that cholinesterase inhibitors can be helpful for psychotic symptoms.^{50,51} Therefore, it is worth considering a trial of this class of drug, especially if significant concern exists about neuroleptic sensitivity. This is also an option if the patient's psychotic symptoms are not severe enough to require urgent treatment and the patient already has an indication for a cholinesterase inhibitor, such as Alzheimer disease or DLB. Cholinesterase inhibitors may also be helpful if the patient has coexisting apathy, since they can be activating.⁵² If depression or anxiety is also present, using an SSRI, such as citalopram or escitalopram, is a good option since an SSRI could treat these symptoms and may be helpful in treating the psychotic symptoms.³⁰

KEY POINT

- It is not useful to argue with patients about the veracity of hallucinations and delusions.

CONCLUSION

Treating responsive behaviors in patients with dementia is both rewarding and challenging. Ultimately, as with other interpersonal interactions, the physician must remember that responsive behavior management requires personal focus and finesse. Adjusting to the trial-and-error nature of treatment requires perseverance in the face of stagnation or regression and the willingness to continue to pursue successful management despite the challenges. The physician's ultimate goal is not to cure the disease but rather to bring the patient's behaviors to a more manageable level. This definition of success can be distressing to the physician who is accustomed to full eradication of disease or symptoms as the primary goal. Maintaining a mindful approach to disease management that uses both pharmacologic and nonpharmacologic strategies will help the physician more effectively manage the behavioral symptoms of dementia.

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