

Chapter 3

Management of Cognitive Function in Older Adults with Dementia



Angela Georgia Catic

Main Points

- Treatment of dementia should be individualized based on patient preferences and comorbidities with consideration given to memory specific medications, management of cardiovascular risk factors, and nonpharmacologic measures.
- Behavioral and psychological symptoms of dementia are common and often have significant implications including institutionalization, increased morbidity and mortality, and significant caregiver burden.
- Nonpharmacologic management is the mainstay of treatment for behavioral and psychological symptoms of dementia. Management plans should be customized to each patient and include generalized and targeted interventions.
- Delirium is more common in older adults with dementia and should be considered within the differential when there is an acute change in cognitive status.

A. G. Catic (✉)

Department of Internal Medicine, Section of Geriatrics and Palliative Medicine, Baylor College of Medicine, Houston, TX, USA

Michael E. DeBakey VA Medical Center, Houston, TX, USA

e-mail: acatic@bcm.edu

Case Vignette

Mrs. CB is an 82-year-old lady with past medical history significant for vascular dementia without behavioral issues, hypertension, and hypothyroidism, who transitioned into a long-term care facility 2 weeks ago. Prior to that time, she was living at home with her daughter. Due to increasing issues with urinary incontinence, Mrs. CB's daughter was no longer able to care for her mother at home. Since transfer to the long-term care facility, the patient is experiencing increasing verbal agitation (calling out), particularly in the evening hours, as well as a reversal of her sleep-wake cycle. Her daughter questions if Mrs. CB's dementia is acutely worsening or if there is another condition else impacting her cognition.

Introduction

Older adults are at increased risk of cognitive dysfunction, with dementia and delirium being among the most common etiologies. Dementia, a general term that encompasses a chronic, progressive decline in cognition (i.e., learning and memory, language, executive function, complex attention, perceptual-motor, and social cognition) which impairs daily function, impacts 1 in 10 individuals over age 65 years or older in the United States [1]. Management of cognitive function in older adults with dementia includes pharmacologic and nonpharmacologic treatment, addressing behavioral and psychological symptoms of dementia, and managing sundowning. When older adults with dementia suffer an acute decline in cognition, it is important to consider the possibility of concurrent delirium. Delirium, defined as an acute disorder of attention and cognition, is more common in patients with dementia and results in significant morbidity and mortality.

Dementia***Epidemiology***

Among older adults, common causes of dementia include Alzheimer's disease, vascular dementia, Parkinson's disease with dementia, Lewy body disease, and frontotemporal dementia. Alzheimer's disease (AD) is the most common etiology of dementia, accounting for 60 to 80% of cases [2]. While rare cases of inherited AD can occur in younger adults, AD is primarily a disease of the aged affecting 15% of individuals ≥ 65 and 45% of those ≥ 85 years of age. The relationship between AD and vascular dementia, the second most common cause (10 to 20% of cases), is poorly understood and a significant number of patients suffer from mixed-etiology

of mixed dementia [3]. Parkinson's disease with dementia (PDD) and dementia with Lewy bodies (DLB) account for up to 30% of dementias [4, 5]. Dementia in patients with Parkinson's disease is classified as PDD versus DLB based on onset in relationship to the onset of motor symptoms (tremor, rigidity, bradykinesia). Dementia developing at least 1 year after the onset of motor symptoms is defined as PDD while dementia developing prior to or within 1 year of the onset of motor symptoms is classified as DLB. Frontotemporal dementia (FTD) is the fourth leading cause of dementia in older adults [6].

Pharmacologic and Nonpharmacologic Treatment

The most commonly utilized pharmacologic treatments for dementia are acetylcholinesterase inhibitors and memantine. Acetylcholinesterase inhibitors (AChEIs) were developed as a result of the cholinergic hypothesis of cognitive decline and function by increasing cholinergic transmission by inhibiting cholinesterase at the synaptic cleft [7]. Donepezil, rivastigmine, and galantamine are approved by the Food and Drug Administration (FDA) for early to moderate AD while donepezil and the rivastigmine patch are also approved in severe AD [2]. In patients with AD, treatment with AChEIs has been associated with improvement in cognitive function, global clinical status, and performance of activities of daily living (ADLs) [8–10]. AChEIs are also first-line treatment in PDD and DLB and, in these subtypes of dementia, studies have indicated they are more efficacious than in AD with positive effects on cognition, psychotic symptoms, and parkinsonian symptoms [11]. This is likely due to the greater cholinergic deficit present in PDD and DLB [12]. While not FDA approved, AChEIs are often used in individuals with vascular dementia. Results of studies evaluating the efficacy have demonstrated small benefits in cognition of uncertain clinical significance [13]. Medications targeting the cholinergic system have not shown significant benefit in FTD [14]. Possible side effects of AChEIs include anorexia, nausea, diarrhea, and bradycardia due to AV block [15]. There is limited empirical evidence regarding discontinuation of AChEIs and considerable variability among practice guidelines [16]. Decisions regarding discontinuation should be made on an individual basis based on patient/family preference, side effects, and financial burden. If treatment is discontinued, the medication should be tapered and cognition reassessed within 3 months so therapy can be reconsidered if a significant decline is detected, understanding that patients may not regain their prior level of function [17].

Memantine, an antagonist at the N-methyl-D-aspartate (NMDA) receptor, was developed secondary to the hypothesized role of the glutamatergic system in neurodegeneration [18]. Memantine is approved for use in patients with moderate to severe AD and, when used in this population, has demonstrated improved cognition, global function, and performance of ADLs [19, 20]. These effects have been demonstrated irrespective of concurrent AChEI therapy [21]. The same benefits have not been demonstrated in patients with mild AD. Among older adults with mild to

moderate vascular dementia, there is low to moderate certainty evidence that memantine results in a small clinical benefit in cognitive function [21]. The evidence for memantine in other etiologies of dementia, including PDD and DLB, is limited. Possible side effects associated with memantine include increased anxiety or agitation, dizziness, and GI symptoms (nausea, vomiting, and diarrhea) [22]. Similar to the AChEIs, discontinuation of memantine should be considered on an individual basis and the medication should be tapered with follow-up assessment of cognition.

Control of cardiovascular risk factors is important in all individuals with cognitive concerns. However, this should be customized to each patient considering their functional status and goals of care. Studies evaluating the impact of statins on preventing cognitive decline or dementia have been mixed. In a review of two randomized controlled trials including 26,340 subjects with moderate to high vascular risk and 11,610 who were ≥ 70 years of age, no difference in individuals developing cognitive decline or dementia was noted between those taking statins versus placebo [23]. Other studies have demonstrated that statins may decrease the risk of developing dementia, especially with long-term use and increasing age [24, 25]. A recent study by Peter and colleagues evaluated the use of statins in 44,920 Swedish dementia patients and determined that individuals on statins had a 22% lower risk of mortality compared to older adults not on statins [26]. The protective effect was more pronounced in younger compared to older individuals (27% versus 20%) and men compared to women (26% versus 17%).

Encouraging meaningful activities in individuals with dementia is important, both for their well-being and that of caregivers. Older adults with cognitive impairment should be encouraged to remain mentally, socially, and physically active. One option for encouraging engagement is attendance at an adult day program. Possible benefits of attendance for the individual with dementia include increased socialization, independence, and simulation based on person-centered activities [27]. Caregivers of older adults attending day programs have demonstrated decreased stress, comfort in the knowledge that their loved one was in a secure environment, and benefit from increased supportive services [28].

Behavioral and Psychological Symptoms of Dementia

Behavioral and psychological symptoms of dementia (BPSD) are defined by the International Psychogeriatric Association as “symptoms of disturbed perception, thought content, mood, and behavior frequently occurring in patients with dementia” [29]. These symptoms are common, impacting 60% of individuals living in the community and 80% residing in long-term care facilities [30–32]. When evaluating BPSD, they can be divided into those with psychotic features and nonpsychotic behaviors (Table 3.1). Medical providers should screen for BPSD during all encounters with older adults with dementia given the significant impact of these symptoms on older adults with dementia and their caregivers. Patients suffering from BPSD

Table 3.1 Behavioral and Psychological Symptoms of Dementia

Psychotic Features	Nonpsychotic Behaviors
Hallucinations Wakeful sensory experiences of content that is not actually present Auditory and visual are most common in patients with dementia	Agitation and irritability
Delusions Strongly held false beliefs that are not typical of a person's religious or cultural beliefs	Inappropriate sexual behavior
Delusional misidentification syndrome Consistent misidentification of persons, places, objects, or events	Sleep disturbances
	Wandering
	Repetitive vocalizations
	Intrusiveness
	Physical aggression

experience increased functional impairment, emotional distress, hospitalization, abuse and neglect, and have decreased survival [33]. Caregivers of individuals with BPSD have increased stress, depression, and economic burden [33, 34]. BPSD is frequently the primary reason for long-term care placement in older adults.

Evaluating Behavioral and Psychological Symptoms of Dementia

Treatment of BPSD begins with taking a thorough medical history and carefully describing the behavior. Providers should inquire regarding medication changes, recent illnesses, mental health issues, substance use, the underlying etiology of dementia, the cognitive baseline, and the functional baseline. A physical exam should be performed and patients should be assessed for the presence of delirium. The importance of describing the behavior is highlighted by the DICE approach (1. Describe the problematic behavior, 2. Investigate possible causes, 3. Create a treatment plan, and 4. Evaluate the outcome of the plan) to manage behavioral symptoms in patients with dementia [33, 35]. Details that should be obtained include a detailed description of the behavior, context, timing, precipitants, and consequences. Providers should also enquire if similar behaviors occurred in the past and what, if any, intervention was effective. While most of the history will be obtained from caregivers, the patient should also be questioned about the episode to see if they can provide further insight into the behavior.

Next, providers should investigate for possible underlying and modifiable causes of the behavior including patient, caregiver, and environmental factors. Patient-related factors include cognitive decline, medication changes, undertreated pain, sleep abnormalities, acute medical issues (i.e., untreated infection, metabolic derangement), sensory deprivation, urinary retention, constipation/fecal impaction, and psychiatric comorbidities. Possible caregiver factors include personal health

issues, substance abuse, and burnout. In addition, a lack of understanding of the disease course and how to most effectively communicate with individuals with dementia may contribute to BPSD. Environmental factors which frequently contribute to BPSD include over or under stimulation, changes in routine, new environment, and lack of meaningful activities.

Nonpharmacologic Treatment of Behavioral and Psychological Symptoms of Dementia

In addition to addressing identified medical issues (i.e., undertreated pain, infection, psychiatric illness, etc.), non-pharmacologic interventions are the primary treatment of BPSD. The medical provider should work with the caregiver and, when possible, the older adult with dementia to develop an individualized management plan that includes generalized and targeted interventions. Generalized interventions focus on improving the environment and caregiver skills [33, 35]. Environmental strategies include removing clutter, reducing loud noises, installing clear lighting, and using simple visual reminders to assist the older adult with common tasks (i.e., picture of the individual on the door to their room, picture of a toilet on the bathroom door). Caregiver strategies include using a caring tone of voice, maintaining a daily routine, avoiding reasoning, and providing simple instructions. Oftentimes, caregivers will benefit greatly from education regarding dementia and BPSD including how to most effectively communicate with older adults with dementia and understanding that behaviors are not intentional. Providers may have resources for caregiver education within their office or can refer caregivers to community resources including the Alzheimer's Association or Area Agencies on Aging. Technology-based intervention, including telehealth technology through which dementia care experts provide in-home support and web-based caregiving interventions, can improve caregiver well-being [36, 37].

Targeted interventions, essential to reducing BPSD, are patient-specific and are essential to reducing BPSD and include cognitive/emotion-oriented interventions, behavioral management techniques, sensory stimulation interventions, and exercise interventions. Some of the most commonly utilized cognitive/emotion-oriented interventions include cognitive stimulation therapy and reminiscence therapy. Cognitive stimulation therapy employs a range of activities (i.e., games, music, dancing, art, gardening, cooking, etc.) to stimulate thinking, memory, and concentration [38, 39]. Evidence suggests that cognitive stimulation therapy may improve memory, thinking, communication, quality of life, and, while data is mixed, possibly reduce BPSD including dementia and anxiety [38, 40, 41]. Reminiscence therapy, an ordered process of reflection on significant life events, uses memory aids (i.e., photographs, music, videos, movies, etc.) to help older adults with dementia recall past events [42]. It can be helpful in reducing symptoms of depression as well as improving communication, retaining, identity, and maintaining self-worth [43, 44].

While a wide variety of behavioral management techniques are used in the treatment of BPSD (i.e. token economies, habit training, positive reinforcement, etc.), the antecedent-behavior-consequence analysis is the basis for the intervention. In this model, the antecedent to the behavior is analyzed and can then either be modified to prevent the undesirable behavior or, if the individual is exhibiting desired behavior, a positive consequence can be used to promote continuation of this behavior. In general, caregivers should focus on reinforcing desirable behavior with positive consequences as this is much more effective and pleasant for the patient and caregiver.

Sensory stimulation interventions, including music therapy, massage, and doll/pet/toy therapy, are frequently used to treat BPSD in older adults with dementia. Music therapy, including music with movement, use of musical instruments, and listening to music, has been associated in some studies with reduced anxiety and agitation, enhanced communication, and increased cognitive functions including speech and attention [45, 46]. Providers can direct caregivers to develop playlists containing music that the older adults enjoy, which can be used to support various activities (soothing versus motivating). Generally, older adults are often most engaged by music that was popular when they were young adults although, as dementia progresses, they may respond most to music from their childhood. While the results of studies evaluating the impact of massage on BPSD are mixed, several have demonstrated decreased stress and agitation among older adults with dementia [47, 48]. While studies evaluating doll/pet/toy therapy in older adults with BPSD are quite heterogeneous, overall results have been positive with evidence of improved quality of life (pet therapy), decreased agitation, and increased pleasure [45].

Physical exercise, defined as planned, repetitive physical activity, is often used in the treatment of BPSD. In a systematic review and meta-analysis of twenty studies evaluating the effect of exercise on BPSD, reduced depression and aberrant motor behaviors were noted [49]. Medical providers should encourage caregivers to assist older adults with dementia in engaging in regular physical activity as allowed by their functional status.

Pharmacologic Treatment of Behavioral and Psychological Symptoms of Dementia

Pharmacologic treatment for BPSD should be considered second-line, only to be considered if nonpharmacologic interventions have failed or the patient's behaviors represent a risk to themselves or others. No pharmacologic therapy is approved by the US Food and Drug Administration (FDA) for the treatment of BPSD and, if providers are going to initiate a pharmacologic therapy, they should start the lowest possible dose and reevaluate tapering or discontinuing the medication on a regular basis. Medications most commonly used in the treatment of BPSD include antipsychotics, benzodiazepines, and antidepressants. Despite the FDA black box warning regarding the use of antipsychotics in older adults with dementia and findings that

they provide modest, if any, benefit compared to placebo, 14.6% of long-stay nursing home residents were being treated with antipsychotics in 2018 [50–52]. If providers initiate antipsychotic therapy for BPSD, it is recommended that they follow the American Psychiatric Association 2016 practice guidelines, which include reserving the medications for when symptoms are severe and dangerous, when non-pharmacologic treatments have already been used, and to taper off the medication in a timely manner (4 weeks in patients with no response and 4 months in patients with a response) [53].

In almost all cases, benzodiazepines should be avoided in older adults with BPSD due to the significant risk of adverse effects including increased confusion, agitation, and gait instability. Possible exceptions include the use of clonazepam for REM behavior disorder and closely supervised use of low-dose lorazepam in cases of significant agitation or aggression resulting in a risk of harm to the patient or others [51].

Although antidepressants are commonly used in the treatment of BPSD, evidence regarding their efficacy for anxiety, depression, apathy, cognition, or care burden is limited [54]. While one study demonstrated a reduction in agitation, the treatment group experienced an increased incidence of cardiac and cognitive side effects [55]. Although mirtazapine is frequently used in older adults in an attempt to improve appetite and sleep, a recent study evaluating the impact of 15 mg of mirtazapine compared to placebo in Alzheimer's patients with sleep disorders demonstrated increased daytime sleepiness but no improvement in duration or efficiency of nocturnal sleep among the treatment group [56]. In addition, the subjects receiving mirtazapine had no improvement in cognition or functional status.

In addition to the more traditionally used pharmacologic therapies, cannabinoids have been suggested as an alternative treatment for BPSD due to activity on the CB1 receptors in the central nervous system. In a systematic review of twelve studies assessing the use of cannabinoids in treating older adults aged 65 year or older with BPSD, observational studies demonstrated improvement in symptoms, but the included randomized controlled trial did not demonstrate an improvement in behaviors [57]. Sedation was the most commonly reported adverse drug event. Future study is warranted before cannabinoids should be considered a standard treatment option for BPSD.

Sundowning

Sundowning, the occurrence of worsening of neuropsychiatric symptoms of dementia in the late afternoon or early evening, is common in older adults with dementia impacting up to 66% of individuals with Alzheimer's disease living at home [58]. Among patients with dementia in long-term care, it is the second most common type of disruptive behavior [59]. Like other dementia-associated behaviors, sundowning is a significant cause of increased caregiver burden and institutionalization. While the pathophysiology of sundowning has not been clearly defined, there are several hypotheses regarding possible etiologies, and experts agree that it is

most likely multifactorial in nature. Possible contributors include alterations in circadian rhythm, degeneration of the cholinergic system, decreased light exposure during the day, afternoon fatigue, reduced caregiver availability in the later afternoon and evening, and certain medications including antipsychotics and antidepressants [59].

While there are currently no validated screening tools for sundowning, it can generally be diagnosed through caregiver history of increased late afternoon/evening behaviors which recur over time and are non-acute in onset [59]. A careful exam to evaluate for physical causes of the behavior, such as pain, should be performed. As in generalized BPSD, nonpharmacologic measures are the first-line treatment for sundowning. Common environmental interventions include light therapy during the afternoon and evening, reduction of excess auditory and visual stimuli, adhering to a routine, and avoiding daytime naps. Caregiver education can also be beneficial so that they are aware of possible sundowning triggers and how to most effectively engage with the older adults with dementia. As in BPSD, pharmacologic therapy for sundowning should only be considered when nonpharmacologic measures have been ineffective. There are no FDA-approved therapies. While melatonin has been noted to reduce sundowning behaviors in older adults with dementia in open-label studies and case series, these studies were heterogeneous and had possible biases [59–63]. There is no evidence to support the use of antipsychotics, benzodiazepines, or hypnotics in the treatment of sundowning [59].

Delirium

Epidemiology

Although increased age is often cited as the key risk factor for dementia, preexisting dementia is also an important independent risk factor associated with a two to five times increased risk of delirium [64]. Impacting up to 50% of hospitalized older adults, delirium is associated with increased cognitive and functional decline as well as institutionalization [65]. In addition, delirium is associated with a significant risk of mortality with patients who are delirious at the time of admission to post-acute care, having a five-times increased risk of mortality at 6 months [66].

Relationship of Dementia and Delirium

While dementia is recognized as an important risk factor for the development of delirium, the relationship between the two conditions is not as well defined. Delirium may unmask previously unrecognized dementia or, secondary to exposure of the brain to noxious stimuli, it is possible that delirium could lead to dementia [65]. Mechanisms proposed for how delirium could lead to permanent neuronal damage include neurotoxicity, inflammation, neuronal damage, accelerated dementia

Table 3.2 Predisposing and Precipitating Factors for Delirium

Predisposing Factors	Precipitating Factors
Age (≥ 75 years)	Medications
Dementia	Infection
History of delirium	Undertreated pain
Functional impairment	Trauma
Sensory impairment (auditory, visual)	Metabolic abnormalities
History of stroke	Surgery
Comorbidity	Restraints
Depression	Lack of assistive devices (glasses, hearing aids, etc.)

pathology, and diminished cognitive reserve [65]. While the relationship of delirium to the development of dementia remains unclear, studies have demonstrated that individuals with dementia who develop delirium have worse outcomes (i.e., hospital readmission, institutionalization, increased mortality) than those who do not develop delirium [65].

Risk Factors and Diagnosis

In older adults, delirium is almost always multifactorial in nature, depending on the interaction of predisposing and precipitating factors (Table 3.2) in vulnerable individuals [64]. Understanding the risk factors for delirium can be helpful as providers counsel patients and families regarding the risk of delirium during scheduled admissions or implement preventative care plans during unanticipated admissions.

Delirium is a clinical diagnosis characterized by an acute onset and fluctuating course of symptoms, inattention, impaired consciousness, and disturbance of cognition [67]. Multiple diagnostic instruments are available including the Confusion Assessment Method (CAM) and the 4 A's Test [68, 69]. Both of these instruments have been validated in older adults and can be administered in a relatively short time in the clinical setting. In a study of 236 patients ≥ 70 years of age admitted to a geriatric medicine ward, the 4AT had a sensitivity of 89.7% and a specificity of 84.1% for detection of delirium [70].

Prevention and Treatment

Nonpharmacologic

The most effective way to prevent the development of delirium in older adults is through the implementation of nonpharmacologic multicomponent approaches.

Common approaches include the Hospital Elder Life Program (HELP) and proactive geriatric consultation [64, 71]. HELP is a multicomponent intervention strategy that implements targeted interventions to address cognitive impairment, sleep deprivation, immobility, dehydration, and vision or hearing impairment. Studies have demonstrated that the program is effective in preventing delirium and functional decline [64, 71]. Proactive geriatric consultation as a means to prevent delirium was studied in patients ≥ 65 years admitted for emergent repair of hip fracture. Structured consultation addressed the following areas: adequate oxygen delivery, fluid/electrolyte balance, pain management, elimination of unnecessary medications, bowel/bladder regulation, adequate nutrition, early mobilization, prevention and treatment of postoperative complications, appropriate environmental stimuli, and treatment of agitated delirium. Compared to the usual treatment group, patients receiving proactive geriatric consultation had a reduced incidence of delirium (relative risk 0.64) [72]. The cornerstone of delirium treatment is addressing the underlying etiologies. In addition, nonpharmacologic supportive measures, including frequent reorientation, supported mobility, reorientation, and sleep protocols should be employed.

Pharmacologic

There is no convincing evidence that pharmacologic treatment is effective in preventing delirium [64, 73]. In addition, the majority of studies have not demonstrated that pharmacologic therapy decreases the duration or severity of delirium [74]. In a systematic review of the use of antipsychotics for treatment of delirium in older adults, there was no decrease in delirium incidence, duration, or severity and no reduction in mortality [75]. If providers chose to use pharmacologic therapy, it should be reserved for patients who are exhibiting severe agitation which places them or those around them at risk.

Case Vignette Continued

Providers at the care facility appreciate the feedback from Mrs. CB's daughter that, prior to admission, she was not calling out and had been sleeping well at night. On assessment, the patient is attentive. Given that her verbal agitation occurs primarily in the evening hours, staff suspect she is suffering from sundowning, primarily related to her recent change in environment. Over the next several days, they make a concerted effort to ensure Mrs. CB is up and engaged in activities during the day, getting a good amount of bright light in the later afternoon and early evening, and having a soothing bedtime routine including herbal tea. With these nonpharmacologic interventions, the patient's behaviors resolve and she successfully adjusts to the long-term care facility.

Conclusion

When managing older adults with dementia, providers should be vigilant for factors impacting their cognitive function. Treatment considerations include memory specific medications, control of cardiovascular risk factors, and nonpharmacologic therapies. Caregivers are a critical component of dementia care and screening for caregiver concerns, including BPSD, should occur at every visit. As BPSD are a common cause of institutionalization, providers should monitor for any behavioral concerns and, if these occur, implement a nonpharmacologic management plan including generalized and targeted interventions. Older adults with dementia are at increased risk of delirium. Providers should counsel patients and caregivers regarding this risk prior to any hospitalization and, if an acute admission occurs, implement multifaceted nonpharmacologic prevention measures.

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