Management of Behavioral and Psychological Symptoms in Dementia

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Management of behavioral and psychological symptoms of dementia (BPSD) is among the most difficult aspects of dementia care and a frequent focus in neuropsychological evaluations. Given that the rate of Alzheimer's disease (AD) is projected to increase exponentially to 7.1 million by 2025, and nearly triple to 13.4 million by 2050 [1], determining effective strategies for the management of BPSD is imperative.

Ineffective management of BPSD has significant negative emotional and functional consequences for the person with dementia (PWD) and his or her caregivers, and is the leading cause of nursing home placement [2]. BPSD often present with a sense of urgency due to distress experienced by the PWD and/or his or her caregivers, and sometimes due to related safety concerns. BPSD are frequently challenging to manage because they often require (a) customization of treatment recommendations, based on a detailed understanding of the problem behavior(s); (b) an iterative, context-dependent approach in determining effective treatment; (c) implementation of some interventions by caregivers; and (d) ongoing follow-up to adjust treatment as behaviors change in the context of increasing cognitive impairment.

This chapter provides a seven-step model for tailoring treatment of BPSD, based on empirically supported strategies from systematic reviews and meta-analyses, and clinical considerations. Pharmacological management strategies are summarized when applicable. Given that AD and AD-related mixed dementias account for 60–80% of all cases of dementia [1], BPSD in AD is a major focus of this chapter. Information on BPSD in other subtypes of dementia is also summarized when applicable.

BPSD Are Common and Persistent

Approximately 60–90% of patients with AD develop behavioral and psychological symptoms including hallucinations, delusions, agitation, dysphoria/depression, anxiety, irritability, disinhibition, apathy, sleep disturbances, and eating changes (3). Multiple studies have shown variable relative frequencies of different types of BPSD. Although mixed research findings make it difficult to determine the most common BPSD, there is great overlap in subtypes of BPSD across studies (see Table 23.1). For example, a recent systematic review and meta-analysis of 48 studies over 50 years showed that the most common BPSD in AD were apathy (49%), depression (42%), aggression (40%), anxiety (39%), sleep disorder (39%), irritability (36%), appetite disorder (34%), aberrant motor behavior (32%),

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Table 23.1 Common BPSD

Apathy
Depression
Agitation/aggression
Anxiety
Wandering
Sleep disorder
Irritability
Appetite disorder
Aberrant motor behavior
Delusions
Disinhibition
Hallucinations

Table 23.2 Tailoring treatment in BPSD: A seven-step model

1: Determine subtype and severity of dementia
2: Specify BPSD symptoms and potential contributing variables
3: Assess and strengthen caregiver engagement
4: Consider increasing daily engagement for the PWD
5: Add customized management strategies based on BPSD subtype, with a focus on behavior therapy
6: Recommend medical consultation
7: Recommend treatment tracking and follow-up

BPSD Behavioral and psychological symptoms of dementia, *PWD* persons with dementia

delusions (31%), disinhibition (17%), and hallucinations (16%) [4]. Another systemic review of 23 studies demonstrated that the most common BPSD are delusions, wandering, agitation, aberrant motor behavior, and apathy [5], while other research showed that apathy, sleep problems, depression, irritability, and wandering were most common [6].

A study examining the relationship between BPSD and mortality over 10 years showed that most BPSD were persistent [6]. However, some BPSD may increase over time, while others may remain relatively stable. For example, a 3-year longitudinal study showed that delusions, hallucinations, agitation, anxiety, apathy, disinhibition, irritability, and aberrant motor behavior increased over time, whereas depression, euphoria, nighttime behavior, and appetite did not [7].

Predictors of BPSD in Different Subtypes of Dementia

Risk factors for increased BPSD in mild AD include younger age, male sex, and greater functional impairment. Increased severity of dementia and frontotemporal dementia (FTD) have also been associated with more BPSD at baseline [7]. Lewy body dementia has been associated with more hallucinations and fewer appetite disturbances as compared to FTD or AD, and AD has been associated with lower levels of BPSD than other dementias at baseline [7]. In AD, lower education has been shown to be associated with

greater distress/tension, and Caucasians exhibited a higher prevalence of affective disorders than other groups [8].

The overall prevalence of BPSD in AD and vascular dementia (VaD) was comparable, and the relationship between higher rates of BPSD and impairment in activities of daily living in AD and VaD was similar, though the types of BPSD differed between groups. For example, patients with AD exhibited more agitation/aggression and irritability/lability than patients with VaD, and AD caregivers reported significantly higher levels of distress. Both groups showed significant associations between impairments in daily functioning and depression, apathy, irritability, and disordered sleep and eating [9].

Tailoring Treatment for BPSD: A Seven–Step Model

A multi-step approach to tailoring BPSD treatment (see Table 23.2), designed for integration into neuropsychology practice, helps ensure consideration of variables that have been shown to impact BPSD treatment success.

Step 1: Determine Subtype and Severity of Dementia

As previously noted, given that different subtypes of dementia are associated with different relative frequencies of BPSD, and given that

BPSD incidence increases with dementia severity, determining the subtype and severity of dementia will help guide the focus on BPSD in the context of the neuropsychological evaluation.

Step 2: Specify BPSD Symptoms and Potential Contributing Variables

Several studies have shown that the success of nonpharmacological interventions in minimizing BPSD is dependent on tailoring the intervention to patient characteristics [10–12]. However, this is often challenging because BPSD may have multifactorial causes that directly impact the expression of symptoms, including neurobiological disease-related factors, unmet needs, caregiver variables, and environmental triggers [13].

As detailed elsewhere [14], a useful framework for specifying BSPD and clarifying potential contributing variables involves two primary steps:

(a) Topographical assessment of BPSD, including
  (a) Identification of target behavior(s) (see Table 23.1)
  (b) Describing the intensity and frequency of target behaviors
(b) Functional assessment of BPSD, including
  (a) Identification of factors that contribute to the etiology of BPSD through examination of the context in which BPSD occurs, with a focus on:
    (i) Factors that precede BPSD ("Antecedents") (e.g. specific situations such as bathing, the presence of others, etc.)
    (ii) Factors that occur after the BPSD ("Consequences"), including adding favorable stimuli (positive reinforcement) or removing aversive stimuli such as task demands (negative reinforcement)
    (iii) "Setting events" that impact antecedents and consequences through contextual factors (e.g. pain, time of day, emotional state, etc.)

Data on these issues can be gathered in the context of the neurobehavioral interview. If there is a desire to obtain more detailed information, several inventories are available to measure these constructs [14].

Step 3: Assess and Strengthen Caregiver Engagement

Caregivers are fundamental partners in supporting effective behavior management and treatment compliance for the PWD. As dementia progresses, the PWD often becomes increasingly dependent on caregiver assistance with daily tasks and oversight of safety. This dependence often shifts the nature of the relationship between the caregiver and the PWD, and may contribute to caregiver stress.

During the neuropsychological assessment, it is often helpful to interview the primary caregiver in person (or via telephone if necessary) to determine the caregiver's insight into the potential need for assistance, their level of engagement in caregiving activities, readiness to implement recommended treatment strategies, and need for support. Caregiver support can be helpful at many time points, but is ideally provided proactively to minimize chronic caregiving stress.

The Alzheimer's Association provides a 24-h Helpline, support groups, and educational information that many caregivers find invaluable on the caregiving journey [15]. Many states also have local Aging and Disability Resource Centers that connect caregivers and PWD with local agencies to assist with management of medications, finances, housework, travel, meals, day programming, and respite services. Connecting caregivers to these and other support services early in the diagnostic process may help enhance caregiver readiness to implement treatment strategies. This may benefit the caregiver and the PWD, given that increased caregiver readiness is associated with a decrease in distressing behavioral symptoms in the PWD and greater caregiver confidence [16].

Beyond connecting caregivers to supportive resources, specific caregiver interventions have been identified as helpful in supporting community-dwelling PWD, including (a) providing opportunities for engagement of both the PWD and the caregiver; (b) encouraging caregiver participation in educational interventions; (c) offering individualized programs rather than group sessions; (d) providing information in an ongoing fashion; and (e) focusing on reducing specific concerning behaviors [17]. Individual behavioral interventions and multicomponent interventions are also helpful in improving the psychological health of caregivers, with the latter intervention also decreasing the rate of institutionalization for the PWD [18].

Step 4: Consider Increasing Daily Engagement for the PWD

Regardless of whether BPSD exist, regular exercise under the direction of a healthcare provider, a routine schedule, and increased engagement in personally enjoyable activities may help improve quality of life for the PWD and, by extension, the caregiver. Recommendations for increasing daily engagement are helpful to make early, at the point of dementia diagnosis (or even when a suspected progressive mild cognitive impairment is diagnosed), to potentially minimize the likelihood and/or severity of current or future BPSD.

Several factors have been shown to increase engagement for PWD. For example, stimuli that are personalized to the interests of the PWD [19, 20] or presented through one-on-one socialization [10] have been shown to be maximally engaging. Engagement in the visual arts has also been shown to be therapeutic for PWD [21], making museum and art programs for PWD and caregivers an increasingly popular activity [22]. In the nursing home setting, dog-related stimuli – including live dogs, puppy videos, and a dog-coloring activity – were associated with increased engagement [20]. In addition, live stimuli (including people) and social (vs. nonsocial) stimuli have been related

to increased engagement [23]. However, the impact of simulated presence therapy [24] and massage/touch in promoting engagement in PWD has been inconclusive [25].

Aerobic exercise is another form of engagement that may assist in decreasing current and future BPSD. In individuals with AD, aerobic exercise has been shown to improve quality of life, psychological well-being, and systemic inflammation [26]. In early AD, aerobic exercise is associated with modest gains in functional ability, cardiorespiratory fitness, and reduced hippocampal atrophy [27], all of which – in addition to the increased fatigue and positive distraction that accompanies aerobic exercise – may help decrease BPSD intensity. Attempting to proactively offset the impact of variables that decrease exercise engagement may also help minimize future BPSD severity. Variables associated with decreased exercise engagement include female sex, older age, and increased medication use, while those associated with increased exercise include higher functional and cognitive status [28].

New directions for increasing engagement in persons with early-stage dementia include the use of positive psychological measures, including constructs of gratitude, life satisfaction, meaning in life, optimism, and resilience, with the goal of developing strength-based psychosocial interventions [29].

Step 5: Add Customized Management Strategies Based on BPSD Symptoms, with a Focus on Behavior Therapy

Individualized behavior therapy has been shown to be helpful in reducing all BPSD summarized below and as such is recommended as a first-line nonpharmacological treatment consideration for agitation/irritability/aggression, depression and anxiety, apathy, sleep disturbance, and wandering. Music therapy also has robust effects in reducing agitation/irritability/aggression, as well as depression and anxiety. Details on these findings and other specialized interventions are summarized below.

Agitation, Irritability, and Aggression

Agitation occurs especially in the middle and late stages of AD [30]. Common behavioral expressions of agitation include excessive psychomotor activity, aggressive behaviors, irritability, and repetitive behaviors. Three psychosocial models have been postulated to explain possible contributors to agitated or aggressive behavior, and suggest that behavior may represent (a) an expression of "unmet needs"; (b) a response to environmental stimuli; and/or (c) a reduced threshold for stress [31]. Examining these potential factors can help refine treatment recommendations.

Nonpharmacological Interventions

Nonpharmacological interventions are recommended as a first-line treatment, unless BPSD symptoms are severe, persistent, or recurrent [5]. Adding pharmacological agents may lead to side effects and increase overall medication burden. In cases of moderate to severe agitation, a combination of pharmacological and nonpharmacological interventions should be considered. Tailoring interventions by examining agitated behaviors from the standpoint of how the PWD may be expressing "unmet needs" has been shown to help decrease aggression [32]. Some research has shown that agitation is the most responsive BPSD to nonpharmacological interventions, as compared to other BPSD including depression, apathy, repetitive questioning, psychosis, aggression, sleep problems, and wandering [33].

Across multiple studies, music has been shown to be a powerful tool in reducing aggressive behaviors. For example, a recent meta-analysis of 12 studies demonstrated that music had clinically and statistically robust effects on agitation (as defined by repetitive acts, restlessness, wandering, and aggressive behaviors; [34]). Similar findings were noted in a recent review of eight randomized controlled trials that showed individualized and interactive music therapy was optimal for management of agitation in institutionalized patients with moderate to severe AD [30]. A recent systemic review of 34 studies provided similar support for individualized music [35].

Music therapy and behavioral techniques were shown to be superior in reducing aggression, agitation, and anxiety, as compared to other therapies including sensory stimulation, cognitive/emotion-oriented interventions (e.g., music/dance therapy, reminiscence therapy, and simulated presence therapy), exercise, and animal-assisted therapy [36]. Another study demonstrated similar positive effects of behavioral therapies in reducing aggression [37]. The relationship between aromatherapy and agitation has also been studied, though findings have been mixed. One study found no significant benefit of aromatherapy in managing agitation [30], though another study showed aromatherapy helped to reduce agitation but not other behaviors such as restlessness/wandering, anger, and anxiety [38].

Engaging with animals, dolls, and robotic animals has also been found to reduce agitation. In a review of 12 studies, doll therapy – a person-centered therapy involving holding, talking to, feeding, cuddling, or dressing an anthropomorphic doll – was found to effectively reduce agitation and aggression [39]. Engagement with animals [40] and a robotic cat was also shown to decrease agitation [41].

Pharmacological and Other Medical Interventions

Although antipsychotic medication is sometimes used to manage agitation in dementia, it has been linked to increased mortality [42], and the use of antipsychotics has declined in light of the black box warning from the Food and Drug Administration [43]. However, the need for effective treatment of agitation has contributed to the study of several other pharmacological agents.

Cholinesterase inhibitors have been shown to be effective in reducing and delaying agitation [3, 44] as well as reducing the need for other medications to manage agitation [3]. Dosage of cholinesterase inhibitors may be an important factor in managing BPSD, based on findings that increasing the dosage of donepezil (from 5 to 10 mg day) improved behavioral symptoms in individuals with Lewy body dementia [45]. Memantine for BPSD in AD has also been

shown to reduce the dose of other medications that are used in managing agitation, including diazepam [46].

Multiple studies have indicated the benefit of citalopram in treating agitation in AD [47, 48], though side effects have also been noted. For example, one study showed that citalopram decreased delusions, anxiety, and irritability after 9 weeks, but increased the severity of sleep behavior disorders after week 9 [49]. Another study found that 30 mg daily of citalopram helped to significantly decrease agitation in AD. However, cognitive worsening was also noted, and it was thus recommended that citalopram 20 mg daily be considered as a first-line treatment in addition to psychosocial interventions [50]. A review of clinical trials evaluating pharmacologic interventions for agitation in AD noted that a range of medications hold promise in treating agitation, including dextromethorphan/quinidine, scyllo-inositol, brexpiprazole, prazosin, cannabinoids, citalopram, escitalopram, and pimavanserin [51].

Electroconvulsive therapy (ECT) is another potential treatment for agitation, based on a study demonstrating that 72% of individuals with acute aggression, agitation, and disorganized behavior secondary to dementia showed a clinically meaningful response to ECT. Maintenance treatment was effective in sustaining the treatment response in 87% of cases, though two cases of significant cognitive adverse effects were noted [52].

Depression and Anxiety

Increased involvement in positive events and enhanced caregiver problem solving have been shown to decrease depression in PWD [53]. Music has also been found to be helpful in treating depression [35, 54, 55] and anxiety [35, 54]. However, the therapeutic benefit of music may depend on dementia severity. For example, in elderly patients with severe dementia, multisensory stimulation environments were shown to reduce anxiety and agitation more than individualized music sessions [56]. Reminiscence interventions were also linked to improved mood,

decreased caregiver burden, decreased dysfunctional behaviors, and reduced institutionalization in AD [37].

In regard to pharmacological management, Citalopram has been shown to be helpful in treating anxiety [49]. However, a 2017 analysis of double-blind randomized controlled trials comparing antidepressants versus placebo for depression in AD found no statistically significant difference between antidepressants (including sertraline, mirtazapine, imipramine, fluoxetine, and clomipramine) and placebo, and concluded that higher-quality randomized controlled trials are needed [57].

Apathy

Apathy is associated with poorer disease outcome, reduced daily functioning, and increased caregiver distress [58]. Apathy is also the most stable and persistent BPSD over 10-year follow-up, and is associated with a threefold increase in mortality compared to other BPSD [6]. Given that disruption of frontal-subcortical networks is likely linked to apathy in AD [59], assessing for the presence of apathy in individuals with frontal subcortical neurocognitive deficits can be informative. Nonpharmacological interventions such as individualized therapeutic activities [60] have demonstrated promise in treating apathy. In addition, short-term occupational therapy was shown to be more effective in reducing apathy than engaging in an activity of choice [61]. Pharmacological agents including acetylcholinesterase inhibitors, gingko biloba, and methylphenidate have been found to help reduce apathy in patients with AD [58].

Sleep Disturbance

Light therapy, increased physical and social activity, and multicomponent cognitive behavioral interventions have been shown to help treat sleep disturbance in dementia [62]. Unfortunately, a recent review on pharmacological management for sleep disturbances in dementia found a lack of evidence to guide drug treatment, including no randomized controlled trials of the many drugs that are widely pre-

scribed for sleep problems and dementia, such as benzodiazepine and non-benzodiazepine hypnotics. There was no evidence that melatonin (up to 10 mg) helped sleep problems in individuals with moderate to severe AD. There was some evidence that low-dose trazodone (50 mg) was helpful, though a larger trial was recommended. There was no evidence of any effect of ramelteon on sleep problems in moderate to severe AD [63].

Wandering

The risk of wandering and getting lost increases as dementia and cognitive impairment worsen. Wandering also frequently creates anxiety, distress, and decreased interactions in PWD [64]. Proactively connecting caregivers to the Alzheimer's Association to learn about the Safe Return registration program [15] can provides support and education about wandering, and more rapid identification of the PWD if wandering occurs. Analyzing patterns related to wandering (e.g., time of day, presence/absence of others, boredom, hunger) can assist in assessing potential "unmet needs" and other variables related to wandering, and provide tailored solutions. Environmental modifications are also often helpful, including disguising locks on doors or doorknobs and using door alarms. Some studies have examined the potential of using global positioning system (GPS) devices to promote safe walking and provide early alerts about potential wandering, though legal issues related to privacy and autonomy are noted [65].

Wandering often increases in residential environments where hallways and/or rooms are undifferentiated. The use of visual cues to assist in wayfinding is beneficial, including the use of colorful, easily identifiable, personally meaningful cues at key environmental decision points such as resident rooms [64]. Other strategies in long-term care settings include environmental modifications (e.g., a secure place to wander, a wall mural, and other visual strategies to disguise exits), music, exercise, structured activities to decrease wandering, and

caregiver education [66]. Environmental modifications are discussed in greater detail in other chapters.

Step 6: Consider Medical Consultation

Medical consultation is often helpful in creating the most effective BPSD treatment plan and helps determine whether BPSD are related to metabolic or other medical issues, and whether adjunctive pharmacological therapy or other medical treatments are warranted. Ongoing communication with medical colleagues about the efficacy of treatment interventions helps ensure that treatments are complimentary and coordinated.

Step 7: Recommend Treatment Tracking and Follow-Up

As previously discussed, caregiver engagement is crucial to treatment success. It is often helpful to recommend that caregivers keep a journal regarding the effectiveness of recommended interventions and are encouraged to share that information with healthcare providers. Caregivers also benefit from having a point of contact for questions that arise between appointments. Caregivers often report feeling more engaged and empowered when they perceive they are part of a team of healthcare professionals and community experts that are dedicated to providing care for their loved one.

Clinical Pearls

- At the point of initial diagnosis of dementia or when a suspected progressive mild cognitive impairment is diagnosed, consider recommending strategies to increase engagement and quality of life for the PWD – including exercise, maintaining a schedule, and engagement in personally enjoyable activities – in

order to minimize the likelihood of current and future BPSD.

- Medical issues should always be ruled out as a contributing factor to BPSD, even if BPSD are chronic.
- An iterative approach to behavioral management is often required before behavior consistently improves, and often necessitates that the caregiver have an ongoing point of contact for treatment input.
- Neuropsychologists are uniquely trained to customize BPSD treatment plans by integrating information from cognitive, psychiatric, and behavioral variables, and would benefit from highlighting this skill to referral sources if this is a desired area of practice.
- When in doubt about what to recommend for BPSD treatment, consider suggesting a behavioral intervention, given that behavioral interventions have the strongest and widest range of support across different subtypes of BPSD.

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