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GERIATRIC DISORDERS (JA CHEONG, SECTION EDITOR)

Managing Behavioral and Psychological Symptoms of Dementia (BPSD) in the Era of Boxed Warnings

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Abstract

Purpose of Review To provide a comprehensive overview on the evaluation and management of behavioral and psychological symptoms of dementia (BPSD) using evidence from literature.

Recent Findings Evidence indicates efficacy for some non-pharmacological techniques including education of caregivers and cognitive stimulation therapy and pharmacological agents like antidepressant and antipsychotics for the management of BPSD. The use of antipsychotics has generated controversy due to the recognition of their serious adverse effect profile including the risk of cerebrovascular adverse events and death.

Summary BPSD is associated with worsening of cognition and function among individuals with dementia, greater caregiver burden, more frequent institutionalization, overall poorer quality of life, and greater cost of caring for these individuals. Future management strategies for BPSD should include the use of technology for the provision of non-pharmacological interventions and the judicious use of cannabinoids and interventional procedures like ECT for the management of refractory symptoms.

Keywords Behavioral and psychological symptoms of dementia (BPSD) · Neuropsychiatric symptoms (NPS) · Neuropsychiatric inventory (NPI) · Non-pharmacological management · Pharmacological strategies · Cannabinoids · Electroconvulsive therapy (ECT)

Introduction

Behavioral and psychological symptoms of dementia (BPSD) also known as neuropsychiatric symptoms of dementia (NPS) include a wide-ranging group of psychological reactions, psychiatric symptoms, and behaviors that are unsafe, disruptive, and confound the care of the individual with dementia in a given environment [1]. Evidence indicates that BPSD tend to occur in approximately one-third of community-dwelling individuals who have a diagnosis of dementia [2]. The prevalence of BPSD increases to almost 80% among individuals with dementia who reside at skilled nursing facilities [3]. Jost and Grossberg in their study found that BPSD occurred in approximately 72% of individuals more than 2 years prior to the formal diagnosis of dementia, with the prevalence of BPSD rising to almost 81%, 10 months after the actual diagnosis of dementia was made [4]. BPSD, unlike cognitive symptoms of dementia which decline over time, tend to fluctuate with agitation being the most persistent symptom [5–7].

Prevalence

The most commonly noted BPSD is apathy and it often occurs early in the illness, and remains stable through the course of the illness [8]. Among individuals with dementia, commonly noted delusions include false beliefs of theft,

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Table 1 Common BPSD

Behaviors/symptoms	Percentage
Apathy	48–92% [8]
Anxiety	21–60% [8]
Delusions	16–70% [8]
Depressive symptoms	30–50% [9, 10]
Disinhibition	Approx.33% [8]
Euphoria	3.5 to 8% [8, 11]
Hallucinations	4–76% [12]
Inappropriate sexual behaviors	7–25% [13]
Mood lability	Approx. 40% [8]
Sleep disturbance	Approx. 25% [14]
Stereotyped behaviors	12–84% [8]
Weight loss	Approx. 20% [15]

infidelity, and misidentification syndromes. Disinhibition is noted in approximately one-third of individuals with dementia [8]. Visual hallucination is the most common form of hallucination among individuals with dementia [8]. Irritability and mood lability become more prevalent as the dementia progresses [8]. Table 1 provides the prevalence rates for common BPSD [8–15]. A family history of depression appears to increase the risk for developing a major depressive episode among individuals with dementia [16].

Neurobiology

Emerging evidence indicates that BPSD occur due to the anatomical, functional, and biochemical changes that occur in the brain of individuals with dementia [17–27]. They can also occur due to the presence of certain genes among individuals with dementia [16, 28–36]. BPSD can occur due to the individual's premorbid personality [37, 38]. Table 2 highlights the various neurobiological changes that are associated with the development of BPSD [17–38].

Consequences

BPSD are a common reason for referral of individuals with dementia for specialist care [39]. It has been noted that BPSD, especially paranoia, aggression, and sleep–wake cycle disturbances, contribute to substantial caregiver burden, increasing the risk for caregiver depression and institutionalization for the individual with dementia [40–43]. BPSD are associated with worsening of activities of daily living (ADLs), faster cognitive decline, and a poorer quality of life for individuals with dementia [2, 44, 45]. After adjusting for the severity of cognitive impairment and other comorbidities, BPSD add to the overall direct and indirect cost of care for individuals with dementia [46, 47].

Assessment

When assessing individuals with BPSD, obtaining collateral information from caregivers is essential [48]. This information will assist in determining the onset, the course of illness, and the differential diagnosis for BPSD [48]. Collateral information also enables the identification of risk and

Table 2 Neurobiology of BPSD

Type	Associated findings
Neuropathology	• The presence of neuritic plaques and neurofibrillary tangles in the frontal and temporal cortices is associated with BPSD [17–20] • Delusional misidentification symptoms (DMS) are associated with atrophy of right frontal lobe [21]
Neurofunctional	• Dysfunction of the frontal, temporal, and parietal cortices is associated with psychotic symptoms [22–26] • DMS is associated with greater EEG delta-power over the right hemisphere [21]
Neurochemical	• BPSD can occur due to damage to cholinergic neurons in the frontal and temporal cortices and to the adrenergic and serotonergic systems [27] • Psychotic symptoms can occur due to higher levels of norepinephrine in the substantia nigra and the lower levels of serotonin in the presubiculum [17, 18]
Genetics	• Depression occurs more commonly in first-degree relatives [16, 28, 29] • 30–61% heritability rate is seen for psychotic symptoms [30] • An earlier age of onset for BPSD is seen in the presence of APOE4 allele [31] • Depressive symptoms can occur in the presence of APOE2 allele [31] • Disorientation, agitation, and motor disorders can be seen among individuals who are homozygotes for APOE4 allele [31] • Individuals with APOE3 allele often present with anxiety and sleep disorders [32] • Visual and auditory hallucinations, hyperphagia, and aggression can occur due to the polymorphisms of serotonin (5-HT2A) receptors [33, 34] • Psychosis and aggression can occur due to the polymorphisms of dopamine receptors [35, 36]
Psychological	• Depressive symptoms are seen among individuals with greater premorbid levels of neuroticism [37, 38]

prognostic factors for BPSD. Additionally, it is important to evaluate the environmental triggers and psychosocial stressors as these may be triggers for the onset or worsening of BPSD. Furthermore, the assessment of comorbid medical disorders including pain syndromes, urinary tract infections, or metabolic disturbances is crucial as these conditions can trigger or worsen BPSD [48].

The use of standardized and validated assessment tools, like the neuropsychiatric inventory (NPI), the Behavioral Pathology in Alzheimer's Disease Rating Scale (BEHAVE-AD), the Consortium to Establish a Registry for Alzheimer's Disease-Behavior Rating Scale for Dementia (CERAD-BRSD), Dementia Behavior Disturbance Scale (DBBS), or the Neurobehavioral Rating Scale (NRS), assists in identifying the different types of BPSD and their frequency and severity. These scales also aid in evaluating their progress and monitoring their response to management strategies. Kales et al. have proposed a structured approach called the DICE (Describe, Investigate, Create, and Evaluate) to assist in the assessment and management of BPSD [49].

Management

For the management of BPSD, both non-pharmacological and pharmacological strategies have been shown to be beneficial [50, 51••]. The most benefit in managing these difficult behaviors is obtained when non-pharmacological and pharmacological interventions are combined [52••].

Non-Pharmacological Management

Available evidence suggests that in most situations, non-pharmacological strategies should be used as first-line option for the management of BPSD [53••]. Livingston et al., in their systematic review, found that the education of caregiver and residential care staff and cognitive stimulation therapy appear to be beneficial in the management of BPSD [54]. They found that visual changes in the environment and the unlocking of doors reduced wandering behaviors, but specialized dementia units were not consistently beneficial to individuals with BPSD. Brodaty and Arasartnam in their meta-analysis found that non-pharmacological interventions provided by the family caregivers tend to reduce the frequency and severity of BPSD (effect size = 0.34, $P < 0.01$) [55]. In addition, these interventions reduced the caregiver burden (effect size = 0.15, $P = 0.006$) [55]. Seitz et al. in their systematic review found statistically significant results in favor of staff training in behavioral management strategies, mental health consultation and treatment planning, exercise, recreational activities, music therapy, or other forms of sensory stimulation as part of non-pharmacological interventions on at least one measure of BPSD [56]. However, many of these studies had methodological limitations and 75% of the studies indicated a need for services from outside of the facility in addition to significant time commitments from the nursing staff for these strategies to be implemented. A recent international Delphi consensus process provided the highest priority to the DICE intervention which evaluates BPSD using a structured method approach, including the assessment of underlying etiologies, planning of care, and follow-up monitoring followed by training and empowerment of caregivers [57].

Pharmacological Management

Emerging evidence indicates efficacy for antipsychotics, antidepressants, anticonvulsant mood stabilizers, cholinesterase inhibitors, and memantine in the management of BPSD [52••]. The next section describes common medication classes that have shown benefit in the management of BPSD.

Antipsychotics

Ballard et al. in their meta-analysis found that risperidone and olanzapine improved aggression among individuals with BPSD when compared to placebo [58]. Additionally, individuals who were treated with risperidone had significant improvement in psychosis when compared to placebo. Schneider et al. in their meta-analysis identified efficacy for aripiprazole and risperidone in the management of individuals with BPSD [59].

In a randomized double-blind, placebo-controlled trial of outpatients with Alzheimer's Disease (AD) and psychosis, aggression, or agitation who were randomly assigned to receive olanzapine, quetiapine, risperidone, or placebo, investigators found no significant difference among the active agents when compared to placebo with regard to the time to discontinuation of treatment for any reason [60]. However, olanzapine and risperidone were favored when compared to quetiapine and placebo in the median time to discontinuation of treatment due to a lack of efficacy. When compared to active agents, time to discontinuation of treatment due to adverse events or intolerability favored placebo. Yury and Fisher found a net effect size of 0.45 for atypical antipsychotics and 0.32 for placebo in their meta-analysis that evaluated risperidone, olanzapine, and quetiapine when compared to placebo for the management of BPSD [61].

Tampi et al. in their systematic review found a total of 12 meta-analyses that evaluated the efficacy of antipsychotic medications in individuals with BPSD [62]. In this review, 10 of the 12 meta-analyses evaluated atypical antipsychotic medications, whereas 2 meta-analyses evaluated typical antipsychotics. The typical antipsychotics were found to have

modest efficacy when used among individuals with dementia, with no superiority noted for any particular medication in this drug class. In addition, risperidone, olanzapine, and aripiprazole showed modest efficacy when used in individuals with dementia including AD. Quetiapine was found to have limited efficacy when used in individuals with dementia. The authors noted that psychotic symptoms, aggression, agitation, and more severe symptoms appear to be particularly responsive to these medications. They noted smaller effects for less severe dementia and those individuals receiving outpatient treatment.

A recent network meta-analysis that included data from 17 studies found that when compared to placebo, the use of aripiprazole, quetiapine, and risperidone was associated with improvements on BPSD [63••]. The investigators did not find any significant difference in effectiveness between the atypical antipsychotics.

Antidepressants

Sertraline and citalopram were associated with a reduction in symptoms of agitation when compared to placebo, in a meta-analysis by Seitz et al. [64]. The authors found that the two studies of trazodone did not detect any difference in BPSD when compared to haloperidol. Both Selective Serotonin Reuptake Inhibitors (SSRIs) and trazodone appear to be well tolerated when compared to placebo, typical antipsychotics, and atypical antipsychotics. Henry et al. in their literature review found a total of 8 trials of SSRIs and 3 trials of trazodone that showed some benefit in the management of BPSD [65]. In 14 of the 19 trials that were reviewed, the antidepressants were well tolerated.

Anticonvulsants

Lonergan et al. in their Cochrane database review found that low-dose sodium valproate was ineffective for the management of BPSD, whereas high-dose divalproex sodium was associated with serious and unacceptable adverse effects [66]. Konovalov et al. in their literature review studied a total of seven RCTs that evaluated the use of mood stabilizers for the management of BPSD. Only one study of carbamazepine showed a statistically significant benefit for the drug-treated group when compared to the placebo, whereas 5 of the 7 studies showed no significant differences among the groups [67]. Adverse effects were noted to be more frequent among the medication-treated groups when compared to the placebo groups in majority of the studies.

Cholinesterase Inhibitors

Trinh et al. in their meta-analysis found that individuals who were treated with cholinesterase inhibitors had modest improvements in BPSD when compared to individuals treated with placebo [68]. The investigators did not find any difference in efficacy between the different cholinesterase inhibitors. Maidment et al. in their meta-analysis found that individuals who were treated with memantine had modest improvements in BPSD when compared to individuals who were prescribed placebo [69]. Sedation was the only adverse event noted more frequently among the drug-treated group when compared to placebo in these studies.

Benzodiazepines

Tampi and Tampi in their systematic review found only five controlled trials that evaluated the use of benzodiazepines for the management of BPSD [70]. These trials were of short duration and with a limited number of subjects. The efficacy data was limited, and the adverse effect profile was not benign with the use of benzodiazepines.

Analgesics

In a systematic review, Tampi et al. identified a total of 3 RCTs that evaluated the use of analgesics among individuals with BPSD [71]. There was evidence of benefit in reducing BPSD in all 3 RCTs. Available evidence indicated that the analgesics appear to be well tolerated in these studies. Supasitthumrong et al. in their systematic review included information from 24 articles [72•]. Data was considered from 15 original case series/case reports that included 87 individuals who were prescribed gabapentin, and 6 who were given pregabalin. In 12 of 15 papers, drug treatment was found to be effective in majority of cases.

Cannabinoids

Emerging evidence indicates efficacy of cannabinoids in the management of BPSD [73]. Tampi et al. in their review of the literature found a total of 8 reports that evaluated the use of cannabinoids for the treatment of BPSD [74]. The investigators included a total of 117 individuals with a diagnosis of dementia, with 58% of these individuals having Alzheimer's type dementia. A total of 7 of the 8 studies indicated improvement in BPSD symptoms with the use of cannabinoids. The symptoms that showed improvement included agitation, aggression, impulsivity, nocturnal restlessness, wandering, and poor sleep. In 4 of the 8 studies, there were no significant adverse effects noted with the use of a cannabinoids. In a systematic review that included data from 12 studies, Hillen et al. found that dronabinol (data from 3 studies) and THC (data from 1 study) improved a variety of symptoms of BPSD [75••]. Sedation was the most common adverse effect reported in these studies.

A Recent Meta-analysis

In a network meta-analysis of 146 RCTs that involved 44,873 individuals with BPSD, Jin and Liu found that aripiprazole, haloperidol, quetiapine, and risperidone showed the most significant efficacy in the management of BPSD, whereas memantine, galantine, and donepezil were thought to have modest effectiveness [76••].

Interventional Procedures

Electroconvulsive Therapy

There is accumulating evidence that electroconvulsive therapy (ECT) is a promising option in the treatment of severe and refractory BPSD [77, 78]. Tampi et al. in their literature review found that there were 20 published reports on the use of ECT for the management of BPSD that included data from a total of 172 individuals with dementia [79]. Majority of the individuals had AD (40%). Bitemporal followed by right unilateral and bilateral were the most common electrode placements. It was noted that over 90% of the individuals responded to ECT treatments. Adverse effects were infrequent and when they occurred, were mild and transient. The most common adverse event noted was postictal confusion/memory impairment that was seen in approximately 15% of the individuals.

Repetitive Transcranial Magnetic Stimulation or Transcranial Direct Current Stimulation

In a systematic review and meta-analysis, Vacas et al. included data from 5 randomized, controlled clinical trials (RCTs) and 2 open-label clinical trial [80•]. The effect of repetitive transcranial magnetic stimulation (rTMS) was evaluated from 5 studies, whereas 2 studies evaluated the effects of transcranial direct current stimulation (tDCS). Two of the 3 RCTs using rTMS showed statistically significant benefits in the management of BPSD, while the 2 studies evaluating tDCS did not find any efficacy for BPSD. A meta-analysis of four RCT studies did not find any evidence of efficacy for noninvasive brain stimulation techniques (rTMS and tDCS), with an overall effect of − 0.02. When the investigators used data from rTMS studies, a benefit was noted with an overall effect of − 0.58. Both rTMS and tDCS were well tolerated with adverse effects being mild and not clinically significant.

Concerns With Using Antipsychotic Among Individuals With BPSD

Cerebrovascular Adverse Events

Concerns about the cerebrovascular adverse events (CVAEs) with risperidone in clinical trials of older adults with dementia was raised for the first time by the Canadian Health Regulatory Agency in 2002 [81]. The Food and Drug Administration (FDA) in 2003 published similar warnings and required changes in the prescribing information for risperidone. In 2004, the European Agency for the Evaluation of Medicinal Products (EMEA) issued a public advisory on the increased risk of CVAEs and mortality in older individuals with dementia who were receiving risperidone. In 2004, the UK's Committee on Safety of Medicines (CSM) advised prescribers that risperidone and olanzapine should not be used to treat behavioral and psychological symptoms of dementia because of "clear evidence of an increased risk of strokes".

In a post hoc analysis of pooled results from eleven randomized controlled trials of risperidone and olanzapine in individuals with dementia, Herrmann and Lanctot found an increased incidence of cerebrovascular adverse events in the drug-treated group when compared to the placebo group [82]. The investigators also found that some of the increased incidence of cerebrovascular adverse events could be accounted for by non-specific events that were not actual strokes. In the risperidone trials, there were a significant number of individuals with vascular and mixed dementias when compared to the olanzapine trials. However, data from two large observational studies found that there was no greater risk of stroke among older adults who were treated with risperidone and olanzapine when compared to those individuals who were treated with typical antipsychotics, or untreated individuals with dementia [83, 84]. A meta-analysis of population-based data found that there was no significant difference in the risk of stroke ($P = 0.96$) among individuals with dementia who were prescribed second-generation antipsychotics when compared to first-generation antipsychotics [85]. A systematic review and meta-analysis of observational studies found that there was increased risk of cerebrovascular accidents (CVA) with first-generation antipsychotics [odds ratio (OR) = 1.49, 95% confidence interval (CI) = 1.24–1.77] but not with second-generation antipsychotics (OR = 1.31; 95% CI = 0.74–2.30) [86]. The risk of CVA (OR = 1.17; 95% CI = 1.08–1.26) with the use of any antipsychotic among individuals with dementia was low.

Mortality

The Food and Drug Administration (FDA) found an increase in mortality with the use of atypical antipsychotics among individuals with dementia [81]. A numerical increase in mortality (1.6–1.7 times) among the drug-treated group was noted when compared to the placebo-treated group from 15 of the 17 placebo-controlled trials of olanzapine, aripiprazole, risperidone, or quetiapine. The deaths were either due to heart-related events (heart failure or sudden death) or infections (mainly pneumonia). A "Boxed Warning" describing the risk of death was added to the labeling of these drugs by the manufacturers, indicating that these drugs are not approved for the treatment of BPSD. More recently, similar changes to the labeling for typical antipsychotics have been added.

The risk of death was found to be greater among individuals who were treated with atypical antipsychotics when compared to placebo in a meta-analysis by Schneider et al. [87]. The investigators did not find any evidence for differential risks for individual drugs, severity of dementia, sample selection, or the diagnosis. Wang et al. in their retrospective cohort study found that conventional antipsychotic medications were associated with significantly higher adjusted risk of death when compared to atypical antipsychotics. This risk remained high for all time intervals studied (< 40 days to ≥ 180 days) and in all subgroups based on the presence or absence of dementia or of nursing home residency [88].

In a review by Mittal et al., the investigators found the risk of death to be about 1.2 to 1.6 times higher in the drug-treated group when compared to placebo group [81]. Data indicated that the risk for death is similar for typical and atypical antipsychotics. The risk of death was associated with older age, male gender, severe dementia, and functional impairment. The risk for death remained elevated for the first 30 days and for possibly up to 2 years.

A meta-analysis from 2018 found that the relative risk (RR) with the use of antipsychotic drugs was approximately 2 for all-cause mortality among older individuals [89•]. The risk period for mortality was highest from the outset and over the initial 0–180 days after starting their use. The risks for all-cause mortality were dose-related; risk increasing with increased doses. There was a small difference noted in the risks when using either the typical or atypical antipsychotics. The risk for mortality was significant and high for all users, including individuals with or without dementia.

A recent registry-based observational cohort study found that the use of antipsychotics at the time of dementia diagnosis was associated with increased mortality risk in the total cohort (hazard ratio = 1.4; 95% CI = 1.3–1.5) [90•]. Increased mortality risk was associated with the use of antipsychotics in individuals with AD, mixed dementia, unspecified dementia, and vascular dementia. A higher risk for mortality was found with typical antipsychotics among individuals with mixed and vascular dementia and with atypical antipsychotics among individuals with AD, mixed, unspecified, and vascular dementia. Furthermore, in patients with AD who had typical antipsychotics, a lower risk of death emerged in comparison with patients treated with atypical antipsychotics.

A Recent Meta-analysis

In a network meta-analysis, Watt et al. found that there was greater risk for cerebrovascular events associated with the use of antipsychotics (odds ratio [OR] = 2.12, number needed to harm [NNH] = 99) and falls associated with dextromethorphan-quinidine (OR = 4.16, NNH = 55) when compared to placebo [91••]. Among subgroup of individuals with AD, the use of antipsychotics was associated with greater risk of fracture when compared to anticonvulsants (OR = 54.1, NNH = 18). Anticonvulsants were associated with greater risk of death when compared to placebo (OR = 8.36, NNH = 35) and when compared to antidepressants (OR = 5.28, NNH = 47).

Possible Algorithm for Managing BPSD

Non-pharmacological strategies have been found to be beneficial to individuals with BPSD and to their caregivers [51••, 54, 55]. In addition, most guidelines recommend non-pharmacological strategies to be the primary intervention for the management of BPSD [53••]. Judicious pharmacotherapy trials can be initiated when the BPSD symptoms are not well managed with non-pharmacological strategies alone [92]. The American Psychiatric Association (APA) practice guideline on the use of antipsychotics to treat agitation or psychosis in individuals with dementia provides a comprehensive document on the evaluation and management of BPSD [93]. Clinicians caring for individuals with BPSD should familiarize themselves with this document in order to follow this guideline and to appropriately care for individuals with BPSD.

As BPSD can emerge or worsen when there is a progression of cognitive decline, it is prudent to start a trial of cholinesterase inhibitors and/or memantine to slow down the process of cognitive decline among individuals with dementia [3]. If possible, the BPSD should then be grouped into different clusters based on the presenting symptoms i.e., psychotic cluster and mood cluster, and these clusters act as psycho-behavioral metaphors of primary psychiatric disorders e.g., psychotic disorders and mood disorders [39].

It is prudent to try and use medications that have known efficacy for similar behavioral clusters e.g., antipsychotics for the psychotic cluster and antidepressants for depressive symptoms in the mood cluster [94].

If symptoms of BPSD are not adequately managed by monotherapy medication trials, a judicious combination of medications can be tried e.g., an antidepressant with an antipsychotic medication or a mood stabilizer with an antipsychotic medication [92]. Prior to starting any new medication trial, those medications that have been found to be ineffective must be tapered and discontinued. Regular monitoring of benefits versus risks of using pharmacotherapy must be conducted to avoid unnecessary medication trials and minimize adverse effects. To minimize serious adverse events, injudicious medication combinations such as two antipsychotics or three or four different medication classes should be avoided. The duration of effective medication trials should be about 3–4 months of clinical stability, following which a trial of medication taper and discontinuation should be initiated [95]. Often multiple different medication trials either as monotherapy or in combination may be needed prior to the amelioration of symptoms [92]. For refractory symptoms of BPSD, cannabinoids and/or ECT should be considered [74, 79].

It is prudent to exercise caution when using antipsychotics among older adults with dementia as they are at high risk for developing serious adverse effects from these medications [81]. Individuals who are at high risk include those who are ≥ 85 years in age, have vascular or mixed dementias or active cerebrovascular or cardiovascular diseases, and significant impairments in activities of daily living. The use of antipsychotics may be justified in these high-risk individuals if the symptoms of BPSD are not sufficiently managed by other strategies [96]. It is also sensible to use the lowest effective dose of antipsychotics and for the shortest period of time when managing BPSD [81]. Potentially serious adverse events can be minimized by the close monitoring of risk factors for adverse outcomes, and their swift management.

There are two published algorithms for the management of BPSD [97•, 98••]. In the first algorithm from Canada, the authors recommend that after completion of a baseline assessment and discontinuation of medications that are potentially exacerbating the BPSD, sequential trials should be done using risperidone, aripiprazole or quetiapine, carbamazepine, citalopram, gabapentin, and prazosin [97•]. The algorithm also provides information regarding titration schedules for medications after adjustments for frailty, the use of ECT, the optimization of cholinesterase inhibitors and memantine, and the use of pro re nata (PRN) medications to manage BPSD. In the second algorithm from the Harvard South Shore, the authors propose three separate algorithms in emergent, urgent, and non-urgent settings [98••]. For emergent BPSD, the authors recommend using intramuscular (IM) olanzapine as first-line treatment (as IM aripiprazole which was previously favored is no longer available). Haloperidol injection is the recommended second choice, followed by possible consideration of an IM benzodiazepine. In urgent setting, the authors recommend using oral second-generation antipsychotics (SGAs)—aripiprazole and risperidone as first-line treatment. The next option could be prazosin, and ECT could be a final option. For non-emergent agitation, the authors recommend the following order of medications: trazodone, donepezil and memantine, antidepressants such as escitalopram and sertraline, SGAs, prazosin, and finally carbamazepine.

Conclusions

BPSD occur commonly among individuals with dementia. BPSD are associated with worse outcomes and greater burden of care among individuals with dementia. BPSD are thought to occur due to the interactions between underlying neuroanatomical and neurochemical changes in the brain and the individual's premorbid personality. The evaluation of BPSD should include a thoughtful assessment of comorbidities, environmental conditions, and psychosocial stressors, as these factors can predispose and precipitate BPSD. The management of BPSD should start with non-pharmacological interventions. The possible benefits of prescribing medications for BPSD should always be carefully weighed against the possible risks of using these medications. Additionally, medications should only be prescribed within the recommended dose ranges to mitigate the risk of serious adverse events. Furthermore, the close monitoring of risk factors will reduce the occurrence of serious adverse events including cerebrovascular events and deaths. Future management paradigms for BPSD should include the use of technology for the provision of non-pharmacological interventions and the judicious use of cannabinoids and interventional procedures like ECT for the management of refractory symptoms.

Compliance with Ethical Standards

Conflict of Interest The authors declare no competing interests.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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