

# Behavioral and psychological symptoms in dementia and caregiver burden

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**Abstract:** Dementia is a mental health disorder of global public health concern. The syndrome of dementia may be caused by various underlying diseases, each characterized by a specific constellation of signs and symptoms in combination with a presumed underlying substrate of neuropathology. Behavioral and psychological symptoms are integral part of dementia. They increase morbidity, influence quality of life and are major source of care giver burden. To be effective, dementia care need to focus on the early detection of BPSD and its management. The spectrum of behavioral and psychological symptoms in different each types of dementia are different and they should be managed accordingly to relieve care giver burden.

**Keywords:** Dementia, Alzheimer's Disease, BPSD, Caregiver, Burden, Vascular Dementia, DLB, FTD, PDD

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## 1. Introduction

Dementia is defined as a considerable decline in cognitive functions that is severe enough to impair the ability to perform personal activities of daily living. Dementia may involve memory impairment, decline in socio-occupational functioning, impaired executive function, speech deficits, personality changes, and behavioral and psychological disturbances. The syndrome of dementia may be caused by various underlying diseases, each characterized by a specific constellation of signs and symptoms in combination with a presumed underlying substrate of neuropathology. Alzheimer's disease (AD) is the most common sub-type of dementia with, approximately two-third of dementia cases over 65 years being diagnosed as AD. The other subtype of dementia includes vascular dementia or multi-infarct dementia (MID), Lewy body dementia (DLB), Parkinson's disease Dementia (PDD), Fronto temporal dementia.<sup>1</sup> Behavioral and psychological symptoms are integral part of dementia. They increase morbidity, influence quality of life and are major source of care giver burden.<sup>2</sup>

### 1.1. Epidemiology of Dementia and BPSD

The World Health Organization (WHO) predicts that by 2025, about 75% of the estimated 1.2 billion people aged 60 years and older will reside in developing countries.<sup>3</sup> In 2005,

it was estimated that more than 24 million people globally and nearly 2 million people in India are affected with dementia.<sup>4</sup>

As per Das et al, rate of growth will be the highest (around 336%) in India, China, South Asia, and western Pacific regions, 235-393% in Latin America and Africa, and the lowest (100%) in developed regions.<sup>5</sup>

In India the number of people with Alzheimer's disease and other dementias is increasing every year because of the steady growth in the older population and stable increment in life expectancy. It is estimated that 4.6 million incident or new cases are added yearly such that the number of people living with dementia will almost double every 20 years to 42.3 million in 2020 and 81.1 million in 2040.<sup>5</sup> Prevalence of dementia was higher in women than in men and nearly doubled with every five year increase in age.<sup>6</sup>

BPSD symptoms are 4 times more common in patients with dementia than older adults without dementia<sup>7</sup>. The prevalence of BPSD in community is estimated to be about 20%<sup>7,8</sup>. The prevalence of behavioral symptoms is greater in nursing homes than in community settings<sup>9</sup> The prevalence of BPSD in the 24 hour care settings has been reported to be as high as 90%, by some studies with individual behaviors including delusions (20%–73%), depression (up to 80%), and aggression and hostility (20%–50%). Nearly 60% of the patients presenting to a memory clinic in one study showed

behavioral disturbances, with psychotic and activity-associated disturbances being the most common presentations.<sup>10</sup>

It has been suggested that BPSD can exhibit variations across different cultures. Preliminary studies of BPSD from India have reported high prevalence rates comparable to most western studies, with caregivers reporting these symptoms as the most distressing and difficult to manage.<sup>11</sup>

### 1.2. Evolution of the Concept of BPSD

Alois Alzheimer initial description of dementia includes behavioral and psychological symptoms of dementia (BPSD) as prominent manifestations of the illness, including paranoia, delusions of sexual abuse, hallucinations and screaming.<sup>12</sup> In 1996, the International Psycho Geriatric Association convened a consensus conference on the behavioral disturbances in dementia. The consensus group made the statement: "The term behavioral disturbances should be replaced by the term BPSD, defined as symptoms of disturbed perception, thought content, mood or behavior that frequently occur in patients with dementia."<sup>13</sup> The BPSD symptoms are listed in Table 1. These broadly conform to BPSD symptoms as described in Cummings' Neuropsychiatric Inventory<sup>14</sup>.

**Table 1. Spectrum of BPSD**

Behavioral Symptoms	Psychological Symptoms
Usually identified on the basis of observation of the patient. They include the following:	Usually and mainly assessed on the basis of mental status examination of patient and interviews with caregivers. They include the following:
Abusive behavior, physical aggression and screaming	Mood disturbances like depressed mood, euphoria, irritability, emotional lability and anxiety
Restlessness, pacing, agitation, wandering	Delusions especially of persecution, reference, misidentification (including Capgras Syndrome).
Culturally inappropriate behavior,	Hallucinations- auditory, visual, tactile and tactile
Sexual disinhibition,	Apathy, amotivation
Hoarding, searching,	Sleep disturbances
Following and shadowing.	Changes in appetite

#### 1.2.1. Categorical Vs Dimensional Approach

While individual symptoms as described above form the categorical approach to BPSD, several authors have found clustering of symptoms which may reflect underlying dimensions. Factor Analysis using NPI have revealed similar set of dimensions in different studies (Table 2) confirming that BPSD is not a homogeneous entity and is best understood as a constellation of dimensions.

**Table 2. Dimensional approaches to BPSD**

Author	Dimensions				
Frisoni et al 1999	Mood			Psychosis	Frontal lobe sx
Fuh et al 2001	Mood- Psychosis				Psychomotor regulation
Aalten et al 2003	Mood- apathy			Psychosis	Hyper activity
Benoit et al 2003	Mood			Hallucination	Psychosis- Agitation
Spalletta 2004	Mood depression- apathy	Anxiety	Mood excitement	Psychosis	Hyperactivity
Mirakhur 2004	Affect		Mania	Psychosis	Physical
Matsui 2006	Mood		Euphoria	Psychosis	-
Chen	Depression- apathy		Euphoria- disinhibition	Hallucination- time behavior	Night Agitation Aggression -Delusion
					Appetite

BPSD is not a diagnostic entity but is instead a term that describes a clinical dimension of dementia.

BPSD can cause tremendous distress for both the patient and the caregiver, and is often the trigger for referral of these patients to primary care and specialist services and placement in residential or nursing home care.<sup>15</sup> The development of BPSD is also associated with a poorer prognosis, a more rapid rate of cognitive decline, illness progression, greater impairment in activities of daily living (ADLs) and diminished quality of life (QOL), and it adds significantly to the direct and indirect costs of care.<sup>16</sup>

#### 1.2.2. Nosological Status

BPSD have not been accorded any diagnostic status in current classificatory systems including ICD-10, DSM 5,

NINDS ARDRA, NINDS AIREN etc which focus exclusively on cognitive symptoms, functional decline and neurological signs.

ICD 10 allows BPSD to be coded as a specifier (predominantly delusional, predominantly hallucinatory, predominantly depressive and other mixed symptoms) with a severity sub specifier.<sup>17</sup>

DSM 5 does allow BPSD to be coded as a behavioral disturbance specifier with sub specifiers of psychotic disorder, mood disorder, anxiety disorder, personality change and sleep disturbance which capture most but not all BPSD symptoms. It also does not accord it any diagnostic or prognostic significance. The issue of psychiatric symptoms versus psychiatric syndrome versus disorder has also not been clarified for BPSD in the context of dementia<sup>18</sup>.

**1.3. Natural History and Course of BPSD**

BPSD symptoms usually fluctuate over the course of dementia.<sup>19, 20</sup>

**1.3.1. Early Stage Dementia Vs Late Stage**

Depressive symptoms often occur in the early stages of dementia. As dementia progresses, other behavioral and psychological symptoms may predominate. Increased cognitive impairment was associated with more activity disturbances, hallucinations, agitation and sleep disturbances; however, delusions, affective disturbances, anxieties and phobias improved with worsening of the cognitive status. Only circadian rhythm disturbances were significantly associated with worsening cognitive status.<sup>10</sup>

Kar *et al* mentioned the association of BPSD with mini mental status examination score (MMSE). In his study, he reported BPSD in 92.5% of patients with MMSE between 11-20 and 84% of patients with MMSE 21-30.<sup>21</sup>

**1.3.2. Persistence Rates**

A study of patients with mild AD found that wandering and purposeless/inappropriate activities persisted or increased in severity over 2 years in about 85% of patients who had these symptoms at baseline, while paranoid ideation persisted in approximately 66% of patients.<sup>22</sup> Hallucinations and depressive symptoms were the least persistent symptoms: less than half of the patients with depressive symptoms still had the symptoms one year later.

**1.4. BPSD and Type of Dementia**

Different Dementias show typical clustering of BPSD (vide table 3). As emergence of BPSD symptoms may precede cognitive decline in a substantial number of cases<sup>23</sup>, such clustering of BPSD symptoms should raise high index of suspicion in clinical practice. However since most symptoms are not specific to a dementia subtype, identification of dementia subtype is often possible only after emergence of cognitive and motor symptoms.

*Table 3. BPSD in different Dementias*

Dementia	Common BPSD	Less common BPSD
Alzheimer’s Disease	Apathy, agitation, wandering, depression, anxiety	Delusions, hallucinations, aberrant sexual behavior
Dementia with Lewy Bodies	Delusions, visual hallucinations, REM sleep behavioral disorder	Other hallucinations
Parkinson’s Disease	Depression, Anxiety, Delusions, hallucinations, REM sleep behavioral disorder	Obsessive- Compulsive symptoms, aberrant sexual behavior
Fronto- Temporal Dementia	Apathy, Disinhibition, Dietary changes	
Progressive Supra nuclear Palsy	Apathy	Disinhibition
Cortico-Basal Degeneration	Depression	Apathy

As many as 80% of Alzheimer’s dementia (AD) patients will develop symptoms of BPSD during the course of their illness, often with the onset of cognitive impairment.<sup>7</sup> Zaudig found that patients with mixed AD and vascular dementia have the highest level of psychiatric disturbances.<sup>21</sup>

Type specific BPSD, e.g; hallucination for DLB, activity disturbances like apathy for FTD, anxiety and phobia for AD and affective disturbances for VaD have been identified<sup>91</sup> in multiple studies.<sup>24</sup>

**1.4.1. Psychotic Symptoms**

Approximately 30–50% of AD patients have been reported to have delusions and hallucinations<sup>21</sup> in one study. Cummings *et al.* (1987) suggested that the frequency of persecutory delusions in multi-infarct dementia (MID) is greater than in AD.<sup>25</sup> The frequency of delusion varies between 10% and 73%.<sup>26</sup> The most common delusions in demented people are persecutory or paranoid.<sup>27</sup> Paranoid delusions in AD have been interpreted as an adaptive response to the cognitive deterioration and the patients’ decreasing ability to grasp and appropriately interpret reality.<sup>10</sup> Other common delusions include Delusion of reference and misidentification including Capgras Syndrome.

Cummings *et al.* (1987) noted a higher frequency of hallucinations in patients with AD<sup>25</sup> while Berrios and Brook (1985) found it comparable in all dementias<sup>28</sup>.

Hallucinations should be differentiated from visual agnosia and misidentification due to poor vision. The frequency of hallucinations in dementia ranges from 12% to 49%.<sup>29</sup> Visual hallucinations are the most common occurring in up to 30% of patients, and these are more common in moderate dementia.<sup>27</sup> In people with Lewy bodies, the frequency can be as high as 80%.<sup>30</sup> Even in AD, Visual hallucinations are more common than auditory.<sup>31</sup>

Several authors have suggested that unlike Functional Psychosis delusions and hallucination in dementia may be part of different subsyndromes.<sup>32, 33</sup> Further, unlike delusions, hallucinations are associated with more severe cognitive impairment.<sup>34</sup>

**1.4.2. Irritability and Aggression**

A study concludes that Aggression and activity disturbances are among the most commonly seen BPSD, and it has been suggested that patients with AD have a higher frequency of aggression.<sup>10</sup>

Physical violence and hitting occurs in approximately 30% of AD.<sup>35</sup> Premorbid aggressions are predictor of aggressive behavior in dementia.<sup>21</sup>

**1.4.3. Mood Disturbances**

Prevalence rates of depression across various types of dementia are controversial, with some investigators reporting a higher frequency of depression in AD compared to other

types, and others reporting the contrary.<sup>36</sup> Depression in patients with dementia stems from neurotransmitter dysfunction associated with the underlying disease process and also from the patients' recognition of the severity of their cognitive impairment.<sup>37</sup> The sudden loss of abilities in VaD can result in an increased incidence of anxiety in the patients.<sup>38</sup> In a study, depressed mood occurs in 40–50% of patients of dementia.<sup>36</sup>

#### **1.4.4. Apathy**

Apathy is present in up to 50% of patients in the early and intermediate stages of AD and other dementias. Apathy may manifest lack of interest in daily activities, self care, social interaction, lack of motivation and initiative and decreased range of affective expression and may be misdiagnosed as major depression. Although lack of motivation occurs in apathy and depression, in apathy amotivation occurs without concomitant dysphoria or vegetative symptoms and is the most common BPSD across all dementia ranges from 75-87%<sup>39</sup>.

### **1.5. Etiopathological Mechanisms in BPSD**

While the origin of BPSD remains unclear; it is presumed there are multiple etiologies for these symptoms. There are neurobiological, psychological (premorbid personality features and responses to stress), and social (environmental change and caregiver factors) aspects in the development of BPSD. The neurobiology of behavioral disturbances involves correlations between memory deficits and decreasing cholinergic function; and between serotonin and noradrenaline depletion and a history of depression or aggression.

There is convincing evidence that the BPSD in AD has identifiable anatomical and biochemical etiological basis. Given the wide array of psychopathologic symptoms in AD, however, it is unlikely that lesions of specific brain structure are related with a specific BPSD.

#### **1.5.1. Neuroanatomical Correlates**

As can be expected, different behavioral problems reflect involvement of different cerebral areas. It has been shown that people with AD who develop psychosis have a 2.3-fold greater Density of NFT (neurofibrillary tangle) in the neocortex (middle frontal, anterior third of the superior temporal, inferior parietal) compared to AD patients who will not develop psychosis<sup>40</sup>.

Brain functional imaging studies have shown that psychosis in probable AD is associated with a reduction in prefrontal, left frontal-temporal, and right parietal metabolism<sup>41-42</sup>. Agitation has been linked to dementia severity, brain-damaged state, various concomitant psychiatric disorders and frontal lobe dysfunction<sup>43-44</sup>. The involvement of limbic system and associated areas as well as cortical hypometabolism have been suggested to contribute to BPSD.<sup>45</sup>

#### **1.5.2. Neurotransmitters**

An imbalance of different neurotransmitters (acetylcholine,

dopamine, noradrenaline, serotonin, GABA) has been proposed as the neurochemical correlate of BPSD<sup>44,46</sup>. Some evidence suggest that BPSD may result from increased norepinephrine (NE) activity and/or hypersensitive adrenoceptors compensating for loss of NE neurons with progression AD<sup>47</sup>.

Dysregulations in GABA (gamma-aminobutyrate)-ergic, serotonergic and noradrenergic neurotransmitter systems have been associated with increased aggressiveness and disturbances in dementia patients.

AD-related apathy is thought to reflect the interaction between cholinergic deficiency and neuropathological changes in frontal brain regions.<sup>48</sup>

In FTD, increased activity of dopaminergic neurotransmission and altered serotonergic modulation of dopaminergic neurotransmission is associated with agitated and aggressive behavior respectively.<sup>45</sup> Studies suggest that, neurochemical mechanisms underlying the pathophysiology of BPSD are specific to the type of BPSD and to the type of dementia and hence more targeted pharmacotherapy may be developed in future.<sup>49</sup>

#### **1.5.3. Genetic Studies**

Genetic studies show that chromosomal abnormalities are a risk factor for the development of BPSD. A relationship between presenilin 1 and psychosis has been demonstrated<sup>50</sup> but not replicated. An association has also been shown between polymorphism of serotonin receptors genes (5HT102-T/C and 5HTCys23Ser) and visual and auditory hallucinations; with the two polymorphisms having an additive effect on visual hallucinations.<sup>51</sup> Polymorphism of the dopamine receptors genes is also involved. A genetic polymorphism of the serotonin transporter promoter region (L/L genotype) has been implicated with aggressive behavior in patients with AD<sup>94</sup>. DRD1, DRD3, SLC6A4 (5HTT) VNTR and 5HTTLPR have been found to be associated with psychosis and aggression/ agitation.<sup>52</sup>

While 5HT2A have been found to be associated with depression, psychosis and aggression/ agitation, 5HT2C have been found to be associated with depression and psychosis but not with aggression/ agitation

APOE E4 been found to be associated with depression and agitation but not with psychosis while COMT has been found to be associated only with psychosis. TPH1 has not been found to be associated with depression, psychosis or aggression in Dementia

### **1.6. Care Giver Burden of BPSD**

BPSD occur in a dynamic process involving the patient, the family caregiver and their environment. They are known to be more stressful to caregivers than cognitive or functional decline, because they are most difficult to manage and have a negative impact on the relationships between the caregiver, patient and family. It has been reported that caregivers differ in their emotional responses to BPSD even when facing similar problems and the caregiver's perception of patient's problems is more important than problematic behavior 'per

se'. Furthermore, caregivers can interpret poorly and react inadequately to BPSD. Caring for dementia sufferers is a highly demanding task both emotionally and physically. Thus, an irritable and sometimes hostile caregiver who easily blames others for the difficulties he/she is experiencing can hardly adapt to a situation of permanent stress such as that of care giving. Furthermore, caregiver personality characteristics may influence the success of intervention programs. Aggressive behavior including physical violence cannot be easily dismissed by caregivers and may make the caregiver fearful of the patient and weaken the caregiver's commitment to ongoing at home care. On the contrary, behaviors that is very difficult to manage, but not directed at the caregiver (e.g., wandering at night), may feel less threatening to the caregiver and result in fewer depressive symptoms<sup>54</sup>. Patient depression is the most frequently reported symptom associated with caregiver depression (35%)<sup>55-60</sup>. Although sleep disturbances (18%)<sup>55, 56, 61</sup>, anger/aggression (12%)<sup>62, 63</sup>, psychosis (12%)<sup>65,68</sup> and agitation (12%)<sup>64,65</sup> were also reported by multiple studies. Depression may be especially challenging for caregivers to handle not only because of the difficulty it causes caregivers in dealing with the patients but also because of the negative impact it has on the patient's quality of life. Anger/aggression (26%)<sup>66,67</sup> and depression (17%)<sup>65,66,68,69</sup> were the most frequently cited patient symptoms having impact on caregiver burden although sleep disturbances (13%)<sup>70,71</sup> and repetitive behavior (13%)<sup>72, 73</sup> were also reported by multiple studies. Shaji *et al* reported that delusions, activity disturbances and aggression were perceived by caregivers to be more troublesome at times than memory deficits. Therefore BPSD may be an important factor predicting the caregiver burden in dementia<sup>74</sup>.

## 2. Conclusion

Behavioral and Psychological Symptoms of Dementia are an important clinical issue and need systematic assessment, management and follow up. Often these are the only symptoms for which effective pharmacological and non pharmacological is available as the core symptoms of dementia may not respond to pharmacotherapy in the long run. As BPSD adversely affect quality of life of both patients and caregivers, hence they should be a focus of further comprehensive research.

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