Behavioral and Psychological Symptoms of Dementia (BPSD) in Alzheimer's Disease: Depression, Anxiety, and Agitation

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Abstract. This study highlights the critical importance of behavioral and psychological symptoms of dementia (BPSD) in the progression of Alzheimer's disease (AD). BPSD—including agitation, depression, and anxiety—are highly prevalent and significantly worsen patients' emotional distress, daily functioning, and quality of life, while also imposing a substantial psychological and economic burden on families and healthcare systems. Despite advances in understanding the pathological mechanisms of AD, the underlying neurobiological processes and the interactions among different BPSD subtypes remain insufficiently understood. This gap limits the development of precise diagnostic markers and practical treatment approaches. Current pharmacological treatments provide only modest benefits and are often accompanied by adverse side effects, underscoring the need for more personalized and comprehensive interventions. Non-pharmacological strategies—such as music therapy, cognitive-behavioral therapy, and regular physical activity—have shown promising effects in alleviating patients' psychological distress and reducing caregiver burden. This study emphasizes that BPSD should be considered a central component of AD management. Future research should prioritize large-scale, longitudinal, and cross-cultural studies integrating neuroscience, psychology, and public health insights to identify more effective and practical intervention strategies, ultimately improving patient outcomes and reducing the long-term impact on families and society.

Keywords: Alzheimer's Disease; BPSD; Neurobiology; Pharmacological Interventions; Non-Pharmacological Interventions.

1. Introduction

Alzheimer's disease (AD) is a progressive and devastating neurodegenerative disorder and one of the leading causes of disability and mortality among older adults. Its hallmark pathological features include the extracellular deposition of β-amyloid plaques and the intracellular formation of neurofibrillary tangles composed of hyperphosphorylated tau protein. These neuropathological changes are strongly associated with the gradual deterioration of memory, cognitive functioning, and activities of daily living. With the rapid global demographic shift toward an aging population, the public health burden of AD is projected to intensify. Estimates suggest that by 2050, more than 15 million people worldwide will be affected. In the United States alone, approximately 6.5 million individuals aged 65 and older currently live with AD, which is expected to double by the end of the century. Such trends present formidable challenges to healthcare systems and impose significant psychological, financial, and social strain on families and communities.

Beyond cognitive decline, AD is characterized by a constellation of behavioral and psychological symptoms of dementia (BPSD), including depression, anxiety, and agitation. These symptoms typically persist throughout the course of the disease, with agitation representing one of the most prevalent and distressing manifestations—occurring in nearly 45% of community-dwelling patients and at even higher rates in institutionalized settings. The International Psychogeriatric Association defines agitation as excessive motor activity, verbal or physical aggression, and marked emotional distress lasting for at least two weeks. Empirical studies have demonstrated that agitation is closely associated with accelerated disease progression, functional impairment, increased hospitalization, and higher mortality, while simultaneously exacerbating caregiver stress and healthcare resource utilization. Although depression and anxiety are also widespread in AD, they have historically received comparatively less attention, and their neurobiological underpinnings remain insufficiently

elucidated. This gap has hindered the development of more effective and targeted therapeutic strategies.

While pharmacological treatments may partially alleviate BPSD, their clinical use is constrained by substantial side effects. Consequently, non-pharmacological interventions are receiving increasing attention. For instance, music therapy has demonstrated benefits in reducing agitation, disruptive vocalizations, resistance to care, and aggressive behaviors, offering feasibility advantages and minimal adverse effects. Moreover, advances in neuroscience have highlighted the role of functional dysregulation in the prefrontal and subcortical regions and aberrant activity within monoaminergic neurotransmitter systems—including norepinephrine, serotonin, and dopamine—in the pathophysiology of agitation. These insights provide promising directions for developing more precise, mechanism-based interventions.

Considering these considerations, the present paper seeks to provide a comprehensive synthesis of depression, anxiety, and agitation as core manifestations of BPSD in AD. Specifically, it examines their clinical presentations, explores underlying neurobiological mechanisms, and evaluates pharmacological and non-pharmacological management approaches. By integrating existing evidence, this study aims to address gaps in the current literature and offer theoretical and practical guidance for clinical care, caregiver support, and future interdisciplinary interventions tailored to the needs of individuals living with Alzheimer's disease.

2. Literature Review

2.1 Pathological Features of Alzheimer's Disease

Alzheimer's disease (AD) has become a significant research focus in contemporary neuroscience and public health due to its profound impact on the global elderly population. As a progressive neurodegenerative disorder, AD is one of the leading causes of dementia among older adults. Pathologically, it is characterized by extracellular β-amyloid plaque deposition and intracellular neurofibrillary tangles formed by hyperphosphorylated tau protein, which contribute to progressive memory loss, cognitive impairment, and decline in daily functioning [1].

2.2 Global Burden of Alzheimer's Disease

The global burden of AD is increasing at an alarming rate. At the beginning of the 21st century, over 35 million people worldwide were afflicted with this disease, and projections suggest this number will nearly double within the next two decades [1]. In Poland alone, over 300,000 older adults are currently affected [1]. Despite this rising prevalence, developing effective diagnostic methods and disease-modifying therapies has not kept pace. Current treatments primarily offer symptomatic relief rather than slowing or reversing disease progression.

2.3 Behavioral and Psychological Symptoms of Dementia (BPSD)

Beyond cognitive decline, Alzheimer's disease is closely associated with behavioral and psychological symptoms of dementia (BPSD), including agitation, depression, anxiety, delusions, and hallucinations. Epidemiological studies indicate that up to 75% of patients exhibit agitated behavior, 60% experience wandering, approximately half display depressive symptoms (such as emotional withdrawal or irritability), 25% engage in shouting or screaming, and about 20% demonstrate aggression or violent behavior [1]. These symptoms intensify patient suffering, accelerate cognitive decline and deterioration in daily functioning, and impose significant emotional and financial burdens on caregivers, often leading to earlier institutionalization.

2.4 Diagnostic Frameworks and Recognition of BPSD

Although behavioral and psychological symptoms of dementia (BPSD) are prevalent, they have not received enough attention in official diagnostic systems. Earlier versions of the *Diagnostic and*

Statistical Manual of Mental Disorders (DSM) mainly focused on memory and thinking problems, and gave little attention to behavioral changes. Later editions, such as DSM-IV, mentioned symptoms like depression, sleep problems, and delusions, but DSM-5 still placed these in a broad category called "with behavioral disturbances" and replaced the term 'dementia' with "major neurocognitive disorder" [2]. This shows a gap between how the DSM describes dementia and the strong research evidence that BPSD is almost always present in Alzheimer's disease and significantly affects patient outcomes. This classification approach has somewhat diminished the recognition and prognostic value of BPSD as an independent clinical phenomenon [2].

2.5 Agitation in Alzheimer's Disease

Among BPSD, agitation is one of the most common and complex symptoms to manage. A systematic review found very different prevalence rates, from as low as 5% to as high as 88%, and nearly 40% of the studies reported that at least half of the patients showed agitation[3]. Long-term studies in European nursing homes also demonstrate how persistent this symptom is. For example, a two-year study in Norway reported a rate of 24.3%[4], and when the same group was followed for four years, the rate rose to 36%[5]. Dutch studies reported incidence rates between 10.9% and 18.2% over two years[6]. However, most of these data come from nursing homes in Europe, so we still know little about agitation among patients living at home or in other parts of the world.

2.6 Research Gaps and Future Directions

While research on BPSD in Alzheimer's disease has increased, most studies still focus mainly on memory loss and agitation, with less attention given to depression and anxiety. Some evidence suggests that changes in brain chemistry and connections in areas like the limbic system and prefrontal cortex may contribute, but these findings are still early and uncertain. Medicines can sometimes reduce symptoms. However, these medications often provide only partial and temporary symptom relief, accompanied by significant side effects [3], highlighting the importance of non-pharmacological interventions. Non-drug methods, such as music therapy, cognitive-behavioral therapy, and exercise, appear helpful for improving patient well-being and lowering caregiver stress. However, more large and systematic studies are still needed. As the global population ages and the impact of Alzheimer's continues to grow, future research should bring together insights from neuroscience, psychiatry, and caregiving. Future research should increasingly adopt longitudinal designs, utilize standardized outcome measures, and integrate interdisciplinary perspectives from neuroscience, psychiatry, and gerontology. This approach will be necessary for developing better, more personalized ways to manage depression, anxiety, and agitation in Alzheimer's disease[1–6].

3. Discussion: Limitations and Future Perspectives

This review highlights the high prevalence and persistence of behavioral and psychological symptoms of dementia (BPSD) in Alzheimer's disease (AD) patients, with agitation, depression, and anxiety being the most common and impactful manifestations. These findings align with previous epidemiological studies, indicating that BPSD is prevalent in AD patients, significantly impacting quality of life, accelerating cognitive decline, and increasing caregiver burden. Therefore, BPSD should be regarded as a core clinical feature of AD rather than merely an accompanying symptom.

Despite growing research, several shortcomings remain. First, the neurobiological mechanisms underlying BPSD remain unclear. Existing studies suggest depression and anxiety may be associated with dysfunction in the prefrontal cortex and limbic system, while agitation may relate to abnormalities in dopamine and serotonin pathways. However, these conclusions lack robust evidence, as most studies focus on single symptoms without exploring interactions between different symptom types. Second, clinical interventions remain limited. Pharmacological treatment is currently the most common approach, yet it often yields only limited and short-term effects while potentially causing side effects such as cognitive decline and metabolic issues. Non-pharmacological interventions like

music therapy, cognitive behavioral therapy, and regular exercise show some positive effects. Still, studies suffer from small sample sizes and inconsistent methodologies, making it difficult to confirm their universal applicability across different populations. Finally, existing evidence predominantly originates from European and American nursing home populations, leaving an insufficient understanding of community-dwelling patients or those from diverse sociocultural backgrounds.

Future research must transcend single-symptom analysis to explore connections between different BPSD subtypes and investigate how genetic predisposition, comorbidities, and environmental factors influence symptom progression. Combining pharmacological and non-pharmacological approaches in treatment may yield more comprehensive and sustained management outcomes. Music therapy aids emotional regulation and social interaction, cognitive behavioral treatment enhances psychological resilience, and regular physical activity may promote brain plasticity and slow disease progression. These approaches require validation through larger-scale, long-term, cross-regional studies employing standardized diagnostic and assessment criteria.

Simultaneously, BPSD burdens not only patients but also caregivers and healthcare systems. Persistent agitation, depression, and anxiety frequently lead to caregiver stress and mental health issues. Societally, it may accelerate institutionalization and increase healthcare costs. Thus, addressing BPSD is not only a clinical imperative but also demands urgent public health attention. Interdisciplinary collaboration—bringing together neuroscience, psychiatry, psychology, gerontology, and public policy—will facilitate the development of more effective, sustainable, and personalized intervention strategies for the future.

4. Conclusion

This study demonstrates that behavioral and psychological symptoms of dementia (BPSD)—particularly agitation, depression, and anxiety—are highly prevalent throughout the progression of Alzheimer's disease (AD). These symptoms not only exacerbate patients' emotional distress and impair daily functioning but also place a considerable burden on families and healthcare systems. Therefore, BPSD should be regarded as a central issue in the management of AD.

Although substantial progress has been made in understanding the general pathological mechanisms of AD, research on the specific causes of BPSD, the interactions among different symptom domains, and their dynamic changes over time remains limited. These gaps hinder a comprehensive understanding of BPSD and constrain the development of more effective and targeted interventions. Future studies should prioritize large-scale, longitudinal, and cross-cultural cohort and randomized controlled trials, employ standardized assessment tools, and incorporate objective indicators (e.g., neuroimaging, sleep, or activity data from wearable devices), while also considering patient quality of life, hospitalization rates, and caregiver burden as primary outcomes.

Overall, this review emphasizes that BPSD are not merely secondary manifestations of AD but a central component of the disease trajectory. By placing BPSD at the core of AD diagnosis and management, and by integrating insights from medicine, psychology, and public health, future research and practice hold the potential to develop more scientific, precise, and humane interventions that can improve the well-being of both patients and caregivers.

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