Depression among Older Adults with Dementia: Double Trouble

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The management of depression among individuals with dementia can be one of the more challenging problems in geriatric practice. Depression in dementia is common regardless of the type of dementia and compounds the impairment of the underlying dementing illness. Some symptoms of dementia, including apathy, impaired concentration, and decreased food intake, may be difficult to distinguish from similar symptoms of depression. This article presents background information on the epidemiology and pathophysiology of depression in dementia followed by recommendations for a systematic approach to diagnosis. Treatment modalities including psychotherapy, pharmacotherapy, and electroconvulsive therapy are reviewed.

Key words: *dementia, depression, Alzheimer's disease, psychotherapy, psychopharmacology*

Introduction

The coexistence of symptoms of dementia and depression in older adults is not uncommon and can be one of the more challenging problems in geriatric practice. This article reviews the complex relationship between dementia and depression in the areas of epidemiology, pathophysiology, clinical presentation, and treatment. The information in this article is intended to help the clinician develop a systematic approach to the diagnosis and treatment of these doubly troubled individuals.

Epidemiology

A common misconception is that depression is universally more common among older adults than in younger age groups. In fact, as determined by the large U.S. Epidemiologic Catchment Area Study as well as other studies, the prevalence of major depression among community-dwelling older adults, 1–2%, is lower than for other age groups.[1,2] Medical illness is a risk factor for depression, and rates of depression are higher in studies of older adults in medical settings. Koenig *et al.* found that as many as 21% of hospitalized older adults fulfilled criteria for major depression, while others have found rates exceeding 25% in many long-term care facilities.[3–5]

Dementia is one of several medical conditions associated with elevated rates of depression. The prevalence of depression in Alzheimer's disease (AD), the most common form of dementia, has been found to be in the range of 17–25%.[6–8] Depression is diagnosed more frequently in mild to moderate AD than in severe AD; however, this may be related to the increased difficulty of elucidating symptoms of depression in individuals with severe dementia.[9] Even higher rates of major depression have been associated with the subcortical dementias including vascular dementia and dementia in Parkinson's disease.[10,11] These rates increase further when those who have depressive symptoms but fall short of meeting criteria for major depression are included.[4]

Pathophysiology

Understanding the mechanisms underlying the increased susceptibility of individuals with dementia to developing symptoms of depression is a goal of current research. One hypothesis is that depression occurs as a psychological reaction to the diagnosis of and limitations from dementia. Research to date has not supported this hypothesis in that rates of depression among individuals with AD do not seem related to their insight into their illness.[6,12,13] Furthermore, one might expect a reactive depression of this sort to follow a course similar to that of the grief reactions of persons with other terminal illnesses. To date, this has not been documented.

A second hypothesis is that the physiological processes responsible for dementia may also play a role in the development of depression. Among individuals with AD and depression, postmortem studies have revealed the loss of noradrenergic cells in the locus ceruleus and the loss of serotonergic nuclei of the dorsal raphe.[6,14–17] The high incidence of depression seen after stroke has led researchers to explore the role of cerebrovascular compromise in depression.[18] Indirect evidence for an association between white matter disease, vascular dementia, and depression led Alexopoulos *et al.* to develop the vascular depression hypothesis, which must be tested by future research.[19]

One of the most controversial hypotheses in the dementia-depression arena is that late-onset depression in an individual without dementia may predict or be a risk factor for the future development of dementia. Bassuk *et al.* concluded that depressed mood did foreshadow future cognitive loss among older individuals but only in those who were already evincing some cognitive difficulties.[20] In contrast, a recent study by Chodosh *et al.* found that high-functioning older adults who experienced depression were at significantly greater risk for

developing cognitive impairment over the following 7 years.[21] The authors review possible mechanisms underlying depression as a risk factor for dementia, including cortisol-induced hippocampal atrophy and chronic inflammation.

In summary, the high comorbidity of dementia and depression has led to hypotheses about shared pathophysiological mechanisms which, while enticing, remain unsubstantiated.

Table 1: Medications Associated with Depressive Symptoms

Medication Type	Examples
Antihypertensives	Beta-blockers, clonidine, methyldopa
Corticosteroids (especially during taper)	Dexamethasone, prednisone, prednisolone
Sedatives, hypnotics	Clonazepam, lorazepam, and others
Hormonal preparations	Estrogen, anabolic steroids
Chemotherapy and immunotherapy agents	Alkylating agents, vincristine, vinblastine, interferon

Clinical Evaluation of the Patient with Dementia and Depression

Present History

Depression remains underdiagnosed among all older adults, not just those with dementia. Among the impediments to diagnosis cited in the literature are fear of stigmatization among older individuals; misinterpretation of somatic symptoms by the clinician; lack of time in the office visit to properly screen for depression; and the belief by some clinicians that depressed mood is a "natural reaction" to the challenges of aging.[22] Clinicians' increased sensitivity to these issues has already resulted in improved rates of detection of depression in the geriatric primary care setting.[23] Screening instruments shown to be practical and effective in the primary care setting include the Primary Care Evaluation of Mental Disorders (PRIME-MD) and the Geriatric Depression Scale.[24,25]

Because of the likelihood that an older adult's dementia will affect memory for recent and remote events, it is crucial that the clinician use, with the patient's permission, additional informants when obtaining the history of present illness. In the outpatient setting, these other informants may include family members and professional caregivers. In inpatient settings, nursing and therapy staff (physical therapists, occupational therapists) often provides important data.

The first step in the evaluation of an older adult with possible depression, with or without dementia, is to rule out possible medical causes. The history should include a review of medications, with attention given to recent prescriptions of medications associated with depression (Table 1).[26] A review of systems should include a careful review of symptoms associated with infection, endocrinopathy, metabolic disorder, and malignancy.

Distinguishing symptoms of depression from those of dementia can be challenging, even for clinicians experienced in this area. A review of the *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition (DSM-IV), criteria for depression (Table 2) reveals that there can be an overlap in symptoms of the two disorders.[27] Apathy has received particular attention in dementia and can be difficult to distinguish from the DSM-IV A criterion of diminished interest.[28] Apathy is among the symptoms of dementia in 40–50% of persons with AD and is also seen among persons with Parkinson's disease and Huntington's disease. It has been associated with frontal lobe impairment, particularly in the area of the anterior cingulate. In clinical practice, persons with apathy who are not otherwise depressed will often feel untroubled by their lack of initiative or motivation, though their family may be alarmed by this development. In contrast, depressed individuals are often troubled by their inability to become interested in usual activities.

Weight loss is another symptom that may be present in both disorders; however, a careful history-taking should be able to elicit whether the weight loss is depression related or part of the underlying dementia. In depression, weight loss is generally associated with a loss of interest in food, an impaired sense of taste, or delusional beliefs that the food may be harmful. In contrast, persons with dementia who lose weight often do so because they forget to eat, lose the ability to obtain food or prepare a meal, or, in advanced dementia, lose the ability to swallow. A person with dementia who experiences anorexia or weight loss and who has recently started an acetylcholinesterase inhibitor medication (donepezil, galantamine, rivastigmine, tacrine) may be experiencing a common side effect of these medications.

Focusing on the symptoms of depression that are unlikely to be mimicked by dementia helps with the diagnosis of depression. A similar approach has been proposed for differentiating symptoms of medical illness from those of depression.[29] These distinguishing symptoms of depression include feelings of guilt, feelings of hopelessness, the belief that one is being punished, and recurrent thoughts of death or suicidal ideation. Provisional criteria for the diagnosis of depression among persons with AD developed by the U.S. National Institute of Mental Health take into consideration those symptoms that help differentiate the two disorders (Table 3).[8]

Suicide rates for older adults are twice those for the general population, and depression is a chief risk factor.[30] Suicide rates among older adults increase with age, but, to date, dementia has not been identified as a risk factor. A common pitfall in suicide risk assessment in older adults is to assume that a debilitated person who is suicidal does not have

Table 2: DSM-IV "A" Criteria for Major Depressive Episode

A.	Five or more of the following for at least 2 weeks and at least (1) or (2):
	1. Depressed mood
	2. Diminished interest or pleasure
	3. Significant weight loss or weight gain
	4. Insomnia or hypersomnia
	5. Psychomotor agitation or retardation
	6. Fatigue or loss of energy
	7. Feelings of worthlessness or guilt
	8. Impaired thinking or concentration
	9. Recurrent thoughts of death or suicide

DSM-IV = *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition.

Source: Reprinted with permission from the *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition, Text Revision, (Copyright 2000). American Psychiatric Association.[27]

the wherewithal to execute a suicide plan. The presence of dementia in an individual with depression does not excuse the clinician from performing a thorough evaluation of suicidal ideation and taking steps to protect a person who is found to be at risk.

Increased tearfulness may be a sign of depression, but it may also be part of a syndrome of uncontrollable laughter or crying referred to as *pseudobulbar affect*.[31] Most often, pseudobulbar affect occurs in persons with AD, but it may also be associated with Parkinson's disease, Wilson's disease, and pseudobulbar palsy.[32] In depression, tearfulness is usually sustained and accompanied by depressive thoughts or mood. Tearfulness associated with pseudobulbar affect, in contrast, is often unpredictable and not associated with sad feelings.

Table 3: NIMH Provisional Criteria for Depression Among Persons with Alzheimer's Disease

A.	Three or more of the depressive symptoms lasting at least 2 weeks and at least (1) or (2):
	1. Depressed mood
	2. Decreased positive affect or pleasure
	3. Social isolation or withdrawal
	4. Appetite disruption
	5. Sleep disruption
	6. Psychomotor agitation or retardation
	7. Irritability
	8. Fatigue or loss of energy
	9. Feelings of worthlessness or guilt
	10. Recurrent thoughts of death or suicide
B.	Symptoms should not be a result of dementia symptoms—e.g., loss of weight due to difficulties with food intake.

NIMH = National Institute of Mental Health.

Source: Adapted from Olin JT, *et al.*, 2002.[8]

Any *abrupt* change in mental status, including a change in mood, should raise a suspicion of delirium in a person with dementia. Persons with dementia, whether because of cholinergic deficits in AD or cerebrovascular disease in vascular dementia, are at increased risk for the development of delirium.[33] They are also at increased risk for medical conditions that may predispose them to delirium, including occult infection and dehydration. Although some individuals with delirium experience psychomotor agitation, others exhibit psychomotor retardation and noncommunicativeness, which may be misinterpreted as signs of depression. Making the distinction is crucial as delirium can be a warning sign of serious medical illness and is associated with increased mortality. The rapid onset of delirium, its waxing and waning course, and the associated fluctuations in consciousness help distinguish it from depression. Dementia, depression, and delirium can present in the same patient, as illustrated in the Venn diagram presented in Figure 1.

Past and Family Histories

Personal history of depression and history of depression among first-degree relatives are both risk factors for developing depression late in life.[34] These histories may not be recoverable from the person with dementia, underscoring the need for ancillary informants, as described above. The clinician should additionally inquire about past symptoms of mania in both the patient and relatives as this may inform treatment decisions.

Physical and Laboratory Evaluations

For an individual with dementia who has

limited ability to provide history, the physical and laboratory evaluations take on added importance. The focus of these evaluations is to rule out medical conditions that may mimic depression or be responsible for a depression with medical origins.

An important element of the physical examination, the mental status examination, should include an evaluation of mood, affect, and thought. *Mood* is the individual's self-report of his or her emotional state. *Affect* refers to the outward manifestation of these emotions. Discordance between the two, for example in a person who describes her mood as "fine" but without warning has bouts of tearfulness, raises a suspicion of pseudobulbar affect. Loss of affect reactivity or affective blunting may be a sign of depression; however, the clinician should be careful not to attribute the flat affect associated with Parkinson's disease to depression. An evaluation of thought content in the depressed individual often reveals themes of nihilism, hopelessness, and guilt. Severe depression may be accompanied by psychotic symptoms including somatic delusions or the belief of having committed an inexcusable offense. An evaluation of suicidal thoughts must include an assessment of whether there is a specific plan and whether arrangements have been made in preparation for its execution.

Laboratory screening continues the process of ruling out possible medical causes (Table 4). Serum chemistry and renal function test results can help rule out dehydration and electrolyte imbalances. The complete blood count can identify anemia, which may present as decreased energy and motivation. Thyroid function testing can rule out hypo- and hyperthyroidism, either of which may mimic depression.[35]

Table 4: Laboratory Evaluation of Depression in Dementia

Serum electrolytes
Complete blood count
Blood urea nitrogen, creatinine
Thyroid-stimulating hormone
Liver function tests, amylase

Key Points

- Dementia is associated with increased rates of depression among older adults.
- Ancillary history obtained from caregivers can be crucial in helping the clinician distinguish signs of depression from those of dementia.
- The history and physical examination should include a review of medical conditions and medications that may induce symptoms of depression.
- Clinicians should take appropriate steps to ensure that dementia-related cognitive impairment does not affect depression treatment compliance.
- Research shows that older individuals with depression respond well to pharmacological treatment and ECT, but data on older adults with dementia are limited.

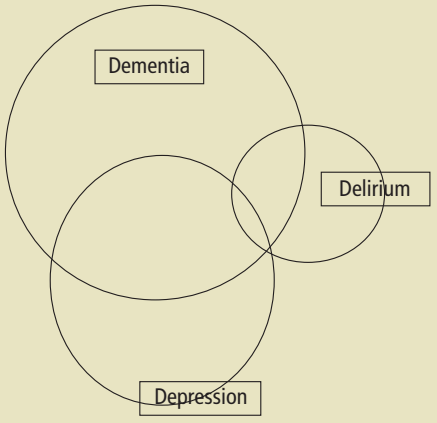
Treatment

Another misconception about persons with dementia and depression is that they are unable to benefit from psychotherapy. A growing body of research argues to the contrary.[36] The choice of psychotherapy depends on the severity of the person's dementia. Relatively intact individuals may benefit from insight-oriented or cognitive behavioural therapy from a therapist who is open to adjusting the process to include a slower pace and more reinforcement. Persons with more severe dementia may still benefit from behaviour therapy[37] as well as individualized art, music, and recreational therapies.

There are few studies on the pharmacological treatment of depression in dementia; most studies on depression among older adults exclude these individuals. As reviewed by Lyketsos and Olin, the available data are contradictory.[6] Because of pharmacokinetic changes associated with aging, prescribing clinicians should adhere to the same principles used with other older adults: start with a low dose, monitor for adverse effects, and slowly titrate the dose upward.[38] Because cognitive impairment can affect medication compliance and because of the several-week response latency that is an inherent part of pharmacotherapy for depression, the clinician needs to confirm that there is a system to ensure that the community-dwelling individual takes the medication as prescribed.

Tricyclic antidepressants are to be avoided as their strong anticholinergic effects can affect cognition as well as other body systems adversely. Selective serotonin reuptake inhibitors (SSRIs) are usually well tolerated and are often used as first-line agents, though paroxetine may also have anticholinergic effects at higher doses. For an individual with Parkinson's disease, an SSRI may exacerbate extrapyramidal symptoms owing to the dopamine-suppression effects of serotonin in the brain system. Such patients may better tolerate bupropion, whose mechanism is dopaminergic and noradrenergic.

Figure 1: Relationships among Dementia, Depression, and Delirium among Older Adult Patients



Electroconvulsive therapy (ECT) has been shown to be safe and effective among older adults,[39] but the data on ECT for individuals with dementia and depression are sparse. Persons with dementia appear to have a higher incidence of post-ECT confusion, but there are no data to raise concerns that ECT worsens or accelerates an underlying dementia. On the contrary, many people experience cognitive improvement when they are freed from the cognitive-impairing effects of major depression.[40]

Conclusion

Depression can compound the disability experienced by persons with dementia. While diagnosing and treating depression can be challenging in an individual with dementia, the effort can be rewarded by improved quality of life and deferment of institutionalization. Additional research is needed to identify effective therapies for this increasingly prevalent condition.

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