Depression and Cognitive Impairment in Older Adults

Depression is primarily a mood disorder, but it can also be viewed as a cognitive disorder for many older adults. In community samples, the co-occurrence of depression and cognitive impairment doubles every 5 years after the age of 70 years, and they are estimated to co-occur among at least 25% of persons older than 85 years. One of the clinical implications of the co-occurrence of depression and cognitive impairment is that there is a higher risk of adverse outcomes for physical health, functional status, and mortality than from each condition alone. Moreover, research suggests that depression in late life may be a prodromal symptom of Alzheimer disease or a risk factor for dementia in general.

The clinical challenge of treating geriatric depression with cognitive impairment is determining the extent to which cognitive changes are caused by depression versus underlying brain pathology. With the growing aging population in the United States and many other countries, it is important for mental health professionals to develop skills to diagnose and treat cognitive impairment in older patients with depression.

For the purposes of this article, our use of the term "depression" refers primarily to symptoms that occur in major depressive disorder (MDD), which is defined as 1 or more episodes of negative mood and sadness sufficient to interfere with daily living. The prevalence of depression is nearly twice as high in women as it is in men. Community-based studies estimate that 30% of individuals first experience depression in later life (at approximately age 60 years), 40% first experience depression earlier in life, and 30% are difficult to categorize reliably because of problems with retrospective recall of past depressive symptoms.

Late-onset depression is more frequently characterized by medical comorbidities, greater apathy, greater cerebrovascular pathology, more extensive cognitive impairment, and a stronger association with dementia. Early-onset depression is more frequently associated with psychiatric comorbidities, family history of mood disorder, and volume loss in the hippocampus when untreated or recurrent.

Although the assessment of cognitive impairment in geriatric depression is predicated on an accurate assessment of depression itself, a full discussion of the clinical assessment of depression is beyond the scope of this article. Table 1 provides a list of elements that are important to a comprehensive evaluation of geriatric depression. In this article, we focus on interviewing and screening for depression, the influence of medical comorbidities on cognitive impairment and depression, and the differentiation of cognitive impairment secondary to depression from comorbid depression and Alzheimer disease.

The neurobiology of depression

Research on the neurobiology of depression has provided important insights into the interrelationship between dysfunctions in mood and cognition. One neurobiological model proposes that a ventral neural system functions to guide affective responses based on the emotional significance and reward value of a stimulus, while a dorsal neural system functions to analyze, monitor, and regulate affective responses to internal thoughts and external events that have high emotional valence.

The ventral system includes the ventral regions of the anterior cingulate gyrus and prefrontal cortex, the amygdala, insula, and ventral striatum; the dorsal system includes the dorsolateral and dorsomedial prefrontal cortices, the hippocampi, and the dorsal anterior cingulate gyrus. Abnormality or damage in the ventral system can lead to decreased motivation and lack of reinforcement from positive experiences, whereas abnormality or damage in the dorsal system can produce dysregulation of emotional responses and exacerbation of negative affect. This broad neural system receives projections from 3 key neurotransmitters linked to depression: serotonin, dopamine,
and noradrenaline. Emotional and cognitive processes are regulated by both systems, and dysfunction in one system may produce dysfunction in the other.

While many persons with depression experience slowed thinking and concentration difficulties, the presentation of cognitive deficits is more heterogeneous among older adults. Depressed elderly persons typically perform worse than nondepressed elderly on neuropsychological measures of information processing speed, 

cognitively demanding processes of selective attention, response inhibition, and performance monitoring (otherwise known as executive functions); and the ability to learn and recall new information. In many cases, these underlying deficits are reflected in a patient's subjective complaints (Table 2).

Neurocognitive deficits involving processing speed and executive functions are more common when first onset of depression occurs in late life, and even more so when apathy is a prominent symptom. In many cases, the combination of slowed processing, executive dysfunction, and apathy are associated with underlying cerebrovascular pathology involving frontal and subcortical brain regions. Other research suggests that older adults with a history of early chronic depression have a more selective deficit in memory, probably caused by reductions in hippocampal volume.

Cognitive impairment

Even though elderly persons who are depressed tend to demonstrate more cognitive deficits than nondepressed elderly, a smaller proportion of depressed individuals have impaired cognitive function. Mild cognitive impairment was first proposed to characterize a state of abnormal cognition with a high risk of progression to Alzheimer disease, but it is increasingly used in depression to characterize depressed individuals with comorbid cognitive impairment in the absence of dementia. The prevalence of mild cognitive impairment in depression ranges from approximately 25% to 50%, which is substantially higher than the 3% to 6% prevalence of conventional mild cognitive impairment in studies of individuals who are not depressed where memory is the focal deficit. An important clinical implication is that mild cognitive impairment or other cognitive impairment during an episode of depression may persist after improvement from the depression symptoms themselves, ranging from one third of individuals with persistent multiple cognitive deficits 1 year after the onset of depression to a 4-fold likelihood for impairments in memory to persist 1 year later among individuals who are in remission.

With or without cognitive impairment, the occurrence of depression in later life is a clinical concern because it may be either a risk factor for or an early symptom of dementia. Several studies have found a higher risk of dementia among persons with a remote history of depression (10 to 25 years before onset of dementia), but they also reveal an increased risk for dementia with decreased time between depression onset and dementia diagnosis, which suggests that onset of depression in later life is either a prodromal symptom or that it creates susceptibility for later dementia. Symptoms consistent with a major depressive episode range from 10% to 30% in patients with mild and moderate Alzheimer disease, with an additional 20% to 30% of individuals having other depression syndromes. Higher rates of depression are seen in patients who have vascular dementia. It is likely that depression is a dementia risk factor for some individuals, while for others it is an early sign of dementia, particularly when the first onset of depression occurs later in life. The key question is which features of affect and cognition best identify which of these respective groups depressed patients fall into.

Diagnosing depression and cognitive impairment

Clinical screening questionnaires should not be used to formally diagnose depression, but they do provide important information to help identify at-risk individuals by characterizing the nature and extent of symptoms that are associated with depression. The Geriatric Depression Scale (GDS) was developed and validated for use with older adults; as such, it avoids somatic and sexual symptoms, surveys subjective experiences of cognitive impairment, and uses simple yes/no items that decrease cognitive burden. A 15-item version of the GDS requires 5 to 10 minutes to complete and is satisfactory for most screening purposes, with a depression cut-off score of 5 or more. Another widely used questionnaire is the Beck Depression Inventory (BDI-II), which was not developed specifically for older adults but is useful because it surveys suicidal ideation and has item content consistent with DSM-IV diagnostic criteria for depression. A score of 15 is often considered to be the lower range of mild but clinically significant depression.

One important but perhaps overlooked aspect of diagnosing either depression or cognitive impairment is a thorough review of risk factors and medical conditions that can be a primary cause or exacerbating element in both these conditions. This is particularly important in geriatric mental health because medical comorbidities are more common in older adults and may have treatable
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Cerebrovascular risk factors are influential in the pathogenesis of both depression and cognitive impairment. One study found that persons with 2 or more cerebrovascular risk factors (diabetes, hypertension, or atrial fibrillation) and lower scores on a neuropsychological measure of executive functions had significantly higher levels of depressive symptoms at baseline and at 18 months compared with persons who had fewer cerebrovascular risk factors and better cognitive performance.47

Other common medical conditions that can cause cognitive impairment include hypothyroidism, which often presents with deficits in memory, visual processing speed, and visuospatial/constructional abilities48; obstructive sleep apnea, presenting with a cognitive profile of psychomotor slowing and deficits in memory, attention, and executive functions49; and vitamin B12 deficiency, which can produce deficits in processing speed and executive functions.50 Several of these conditions (eg, hypothyroidism) can produce depression or behaviors consistent with depression, such as lethargy and fatigue from B12 deficiency, and dysphoria, concentration deficits, and apathy in the context of sleep apnea.

Medication review is also important because depression symptoms have been associated with common medications including α-methyldopa, amantadine, β-blockers, β-interferon, calcium channel blockers, clonidine, metronidazole, prazosin, reserpine, and steroids.51 Deficits in memory and information processing speed have also been associated with benzodiazepines52,53 and tricyclic antidepressants, particularly amitriptyline.54

Several features of the presentation and clinical history of depressed older adults can help clinicians differentiate between a major depressive episode and Alzheimer disease. Table 3 lists differences in the clinical and cognitive presentations of depression and dementia, including the core distinction that cognitive deficits associated with depression generally emerge and remit in concert with mood changes on a timeline of weeks to months. In contrast, cognitive changes in dementia are more independent of mood symptoms and become progressively worse over a timeline of months to years. Table 4 [Table restricted. Please see print edition for content.] summarizes the distinction between diagnostic criteria for a major depressive episode and depression in Alzheimer disease. It is important to recognize that patients with depression may appear cognitively impaired because they tend to give up easily or produce "I don't know" responses to complex questions or those that require effortful recall. Alzheimer disease may be more likely if the quality of a patient's responses does not improve with increased time to respond or with memory cues. It is also important to carefully assess functional activities to determine whether deficits are caused more by loss of knowledge or ability (Alzheimer disease) or whether they are caused by loss of interest or motivation (depression and some dementia).

Given the possibility of impairments in reporting cognitive and functional behaviors, clinicians should try to obtain collateral information from family members, particularly with suspected dementia, where family is often the first to notice subtle cognitive changes. A quick and useful informant-based screening of cognitive decline and dementia is the Informant Questionnaire on Cognitive Decline in the Elderly.55,56

Clinical screening of cognition is important to identify depressed patients with overt cognitive impairment, but it presents a number of limitations for differential diagnosis and early detection of dementia. Many clinicians use a score of 24 or lower on the Mini-Mental State Examination (MMSE)57 to identify impairment, but this may miss many persons with milder impairment because the MMSE has a low ceiling of difficulty; a limited assessment of processing speed and executive functions; and differential sensitivity to age, education, and ethnicity.58

In our clinical experience, we have seen a number of high functioning, well-educated individuals with perfect MMSE scores and a diagnosis of mild cognitive impairment based on more extensive testing. However, we have also seen many individuals with low literacy and education levels for whom a score of 24 is a reflection of their normal function.

Deficits on cognitive screening or persistent patient or family reports of cognitive difficulty despite improved depression should be followed up with additional clinical assessment and often a neuropsychological evaluation to more fully characterize the severity and extent of cognitive deficits. Neuropsychological evaluations can be useful in distinguishing prefrontally mediated deficits in memory retrieval that characterize a cognitive syndrome of depression from those hippocampally mediated deficits in memory consolidation and storage that characterize early Alzheimer disease (Table 3).59 An evaluation can also help differentiate depression in Alzheimer disease from other dementias that commonly present with depressive symptoms.

Early detection of dementia with the aid of neuropsychological assessment helps promote early...
intervention and allows tracking of cognitive change in response to treatment. Serial neuropsychological assessments of cognitively impaired individuals can help estimate whether cognitive deficits have partially or fully resolved (as in depression and some medical conditions), have remained stable (as in cerebrovascular events), or have been progressive (as in Alzheimer disease or other dementing disorders).

**Treatment options**

Psychiatric treatment of individuals with both depression and cognitive impairment requires consideration of both the affective and cognitive elements. In the Depression in Alzheimer Disease Study, sertraline was found to be effective in treating individuals with comorbid major depression and Alzheimer disease. In addition, individuals who responded well in mood also improved in activities of daily living and behavioral disturbances not associated with mood, but cognitive function did not improve in conjunction with mood. There is no current evidence to recommend treating cognitive impairment in MDD with medications for Alzheimer disease; in fact, starting both an antidepressant medication and a cognitive medication may complicate the clinician’s ability to manage side effects and adverse events. Persistent or worsening memory deficits after several months of remission or mild depression raise suspicion of dementia, in which case prescription of cholinesterase inhibitors (eg, donepezil, galantamine, rivastigmine) or an N-methyl-d-aspartic acid receptor antagonist (eg, memantine) may be beneficial. Pharmacological treatment of geriatric depression with cognitive impairment is complicated by the fact that deficits in executive functions are associated with lower remission rates and higher recurrence of depression. Psychotherapy may mitigate some cognitive deficits associated with depression, as evidenced in a study that found a 12-week trial of problem-solving therapy was associated with higher remission and lower functional disability compared with supportive therapy when used with depressed older adults who had comorbid deficits in executive functions. What is interesting about this study is that the focus on practical problem-solving strategies appeared to be beneficial to individuals whose cognitive deficits compromised their ability to resolve psychosocial aspects of depression.

Cognitive impairment and depression are common among older adults, and the combination of these 2 conditions may lead to persistent difficulties with both cognition and mood. Clinicians can reduce the occurrence of complicating factors with a proactive approach to evaluation that includes effective detection of cognitive impairment and referral for more comprehensive assessment when indicated. Treatment approaches should be similarly proactive and may include a combination of pharmacological and psychotherapeutic interventions.
References:

20. Sheline YI, Barch DM, Garcia K, et al. Cognitive function in late life depression: relationships to...


47. Mast BT, Yochim B, MacNeill SE, Lichtenberg PA. Risk factors for geriatric depression: the


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