Neurologic Changes and Depression

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KEYWORDS

- Major depressive disorder
 Subjective cognitive impairment
- Mild cognitive impairment
 Neurocognitive disorder
 Neuropsychological testing
- Neuroimaging
 Psychotherapy
 Antidepressants

KEY POINTS

- The assessment of late-life depression with comorbid cognitive impairment can be challenging and requires a clear clinical history and a thorough medical and cognitive assessment.
- There are several neuropsychological changes associated with late-life depression, ranging from subjective cognitive complaints to mild cognitive impairment to dementia.
- Changes on neuroimaging and in several biomarkers (eg, apolipoprotein E e4 allele, betaamyloid, tau, neurotrophins, and so forth) have been associated with late-life depression.
- Multiple psychotherapeutic techniques have been found effective in the treatment of latelife depression as well as holistic/nontraditional, pharmacologic, and brain-stimulation approaches.

INTRODUCTION

Late-life depression affects 3.0% to 4.5% adults older than 65 years in the United States. For many older adults with depression, affective symptoms are accompanied by cognitive difficulties, which can range from subjective cognitive complaints to mild cognitive impairment (MCI) to dementia. Epidemiologic findings suggest that late-life depression may be a risk factor for dementia. Given the relatively high prevalence of depression in older adults and a growing focus on modifiable risk factors for dementia, there is interest in better understanding the complex relationship between depression and cognitive impairment. This review focuses on individuals with unipolar depression without psychotic features with comorbid MCI or dementia. To align with the

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terminology used in earlier literature and within the *International Classification of Diseases, Tenth Revision* coding system, the authors use *Diagnostic and Statistical Manual of Mental Disorder* (Fourth Edition, Text Revision) (*DSM-IV TR*) terminology (ie, MCI and dementia) instead of the *DSM-5* terminology for neurocognitive disorders.

Clinical Assessment of Late-Life Depression with Comorbid Cognitive Impairment

Accurately diagnosing late-life depression can be challenging because of the wide variety of symptom presentations. ⁴ A few key points can guide the clinical evaluation of depression in older adults with comorbid cognitive impairment. Specifically, these are (1) receiving a detailed history from both the patients and their informants, (2) following patients longitudinally to monitor symptom progression, and (3) interviewing with potential reversible causes of cognitive impairment in mind (eg, substance use, metabolic problems, and so forth).

First, the most powerful diagnostic tool the clinician has is the clinical interview. Obtaining a detailed history from both the patients and their informants will be a critical piece to determine whether the patients have a primary mood and/or cognitive disorder. In certain cases, a detailed neuropsychological evaluation may be necessary to delineate cognitive and mood symptoms. Furthermore, neuropsychological testing is indicated when there are questions of multiple comorbidities, questionable selfor informant-report, and to establish a baseline in mild dementia and MCI cases. An accurate informant can be especially helpful, as many patients frequently experience anosognosia (lack of awareness due to neurologic disease) about their cognitive deficits or alexithymia (inability to describe one's feelings). Patients may also experience variations in their mood depending on the time of day (ie, diurnal variations); therefore, an informant may be helpful in mapping the overall mood.

Second, clinicians can follow patients' symptoms over time. This technique can be important in the diagnosis of more complex cases when it is difficult to determine whether patients' have primary cognitive disorder, primary mood disorder, or both. Clinicians should determine whether emotional and cognitive symptoms resolve, remain static, or progress over time. For example, if the cognitive symptoms worsen despite stable or improved mood, this would suggest a primary cognitive disorder. Alternatively, if the cognitive symptoms vary with emotional state, for example, worsening with increased emotional distress, this would suggest a primary mood disorder.

When patients present with both significant emotional and cognitive complaints, clinicians should aggressively treat the depressive symptoms first and then reassess cognitive symptoms after some resolution of the severe emotional distress. Literature has indicated that mild to moderate depression is best treated with a combination of antidepressants and psychotherapy. However, the patients' cognitive capacity to engage in psychotherapy should always be considered. Electroconvulsive therapy (ECT) and other brain-stimulation therapies are generally reserved for severe or treatment-resistant cases.

Third, clinicians should always approach these complex cases considering potential reversible causes of the patients' mood and cognitive symptoms. One of the most overlooked, but easily reversible, causes of cognitive impairment in older adults is medication side effects. Specifically, research has shown that benzodiazepines, anticholinergics, opiates, non-narcotic pain medications (ie, tramadol), hypnotics, and antipsychotics have been associated with cognitive symptoms. Substance use in older adults is frequently not explored thoroughly, particularly in regard to alcohol and cannabis use. Finally, a thorough workup for late-life depression should also include a comprehensive laboratory workup, assessing hematologic, metabolic, toxic, and infectious contributions to cognitive and/or affective symptoms.

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