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INVITED REVIEW

Geriatric depression and cognitive impairment

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Cognitive impairment is common in geriatric depression, and depressed individuals with co-morbid cognitive impairment are at increased risk for a number of adverse medical, psychiatric and cognitive outcomes. This review focuses on clinical issues surrounding the co-occurrence of these two conditions within the context of current research. We (1) review the clinical criteria and prevalence of depression, as well as co-morbid cognitive impairment, (2) discuss factors associated with persistent cognitive impairment in depression, including dementia, and (3) review research relevant to the assessment and treatment of cognitive impairment and dementia in the context of depression. We conclude that current research on depression and cognition can inform clinical decisions that reduce the occurrence of adverse outcomes. Clinicians are encouraged to develop proactive approaches for treatment, which may include combinations of pharmacological and psychotherapeutic interventions.

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Introduction

Although depression is generally characterized as a mood disorder, there is increasing recognition that it is also a cognitive disorder for many older adults. Viewed separately, clinically significant depressive symptoms are present in 11–30% of older adults internationally (Kivela *et al*. 1988; Gallo & Lebowitz, 1999; Steffens *et al*. 2000; Copeland *et al*. 2004; Lee & Shinkai, 2005), and cognitive impairment is estimated to exist in 17–36% of adults over the age of 65 (Koenig & Blazer, 1992; Lee & Shinkai, 2005; Rait *et al*. 2005; Graciani *et al*. 2006). Community samples demonstrate doubling of co-morbid cognitive impairment and depression at each 5-year interval after the age of 70 years to the point that this combination is present in 25% of 85-year-old subjects (Arve *et al*. 1999). Co-morbid depression and cognitive impairment is a particular clinical concern because it increases the rate of adverse outcomes for physical health, functional status and mortality (Mehta *et al*. 2003). Given that the personal and public burdens of both depression and cognitive impairment are likely to increase along with the aging populations of most industrialized nations, it is important for mental health professionals to better understand the characteristics, detection and treatment of cognitive impairment in depression.

This review examines key research and clinical issues associated with cognitive impairment and depression, with a focus on late life. After reviewing the clinical criteria and prevalence of depression, we examine the occurrence of cognitive impairment within this condition. Next, we discuss clinical features that may be associated with either a specific etiology or a likely clinical course of depression, and also review the factors associated with the persistence of cognitive impairment in depression, including dementia. We then address the status of current research on key issues in the clinical assessment and treatment of co-morbid cognitive impairment and depression.

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Depression

Depression is mood disorder that produces sadness, negative self-regard, loss of interest in life, and disruptions of sleep, appetite, thinking and energy level. These symptoms are classified as a depressive episode in both international (ICD; Dilling *et al*. 1991) and American (APA, 2000) diagnostic systems when they are present for more than 2 weeks and interfere with daily living. Although diagnostic criteria encourage the categorization of specific subtypes and severity levels of depression, it is important to recognize that any depressive symptoms that impair cognition or activities of daily living (ADLs) are clinically significant (Koenig & Blazer, 2004). In this review, the use of the term *depression* includes any constellation of depressive symptoms that is sufficient to impair cognition, social functioning or other important aspects of daily living, and we refer to the term *major depression* where it is important to make this clinical distinction.

Depression and neurocognitive function

Although dysfunction in concentration is one of the key diagnostic criteria of depression, the presentation of cognitive deficits is heterogeneous. While many depressed individuals have no cognitive complaints or objective findings on neurocognitive assessments, most research on neurocognitive function in depression has found that depressed individuals tend to have worse performance relative to non-depressed comparison groups on a number of neuropsychological measures (Veiel, 1997; Zakzanis *et al*. 1998), with the most consistent deficits occurring in the areas of processing speed (Nebes *et al*. 2000; Sheline *et al*. 2006); effortful tasks involving selective attention, response inhibition, and performance monitoring (i.e. executive functions) (Boone *et al*. 1995; Beats *et al*. 1996); and the acquisition and retrieval of new information (i.e. episodic memory) (Beats *et al*. 1996; Austin *et al*. 1999). Deficits in information processing speed and executive functions appear to increase with severity of depression symptoms, particularly apathy (Boone *et al*. 1995; Feil *et al*. 2003). Neurocognitive deficits involving executive dysfunction are more common when first onset of depression occurs in late life and even more so in the presence of vegetative symptoms (Palmer *et al*. 1996); however, some research suggests that memory deficits may be more focally affected among older individuals with a history of recurrent depression beginning earlier in life (Rapp *et al*. 2005).

The cognitive neuroscience of depression

Cognitive neuroscience has made important contributions to understanding how specific neural mechanisms in frontal and subcortical regions are associated with specific characteristics of cognitive processing among depressed individuals. This in turn provides insight into cognitive impairments that may occur as a result of brain changes in regions associated with depression. Although depression is influenced by a number of brain regions within larger neural systems (Phillips *et al*. 2003), we focus on four key regions: (1) the orbitofrontal cortex, (2) the anterior cingulate gyrus, (3) the dorsolateral prefrontal cortex, and (4) the hippocampus.

The orbitofrontal cortex (OFC) appears to have a cognitive role in the selective processing of affective stimuli, and is associated with the finding that depressed individuals show a more rapid reaction to sad words than to happy words (Elliott *et al*. 2002). The OFC is also associated with a disproportionate response to negative feedback that is evidenced on tests involving learning of stimulus–reward associations (i.e. reversal learning) (Murphy *et al*. 2003), which makes depressed individuals predisposed to cognitive errors if they have received negative feedback on preceding tasks. Structurally, neuroimaging studies have found smaller total OFC volumes, smaller OFC gray matter volumes, and more prominent hyperintense lesions in elderly depressed individuals relative to non-depressed (Lai *et al*. 2000; MacFall *et al*. 2001; Ballmaier *et al*. 2004).

The cognitive role of the anterior cingulate gyrus (ACC) appears to involve both initiation (Nemeth *et al*. 1988) and suppression (Paus *et al*. 1993) of behavior through conflict monitoring (Carter *et al*. 2000) and appraisal of motivational content (Devinsky *et al*. 1995). In this role, the ACC is involved in the affective processing bias seen in depression, in which depressed individuals responding more rapidly to sad *versus* happy words also demonstrate an elevated neural response in the rostral anterior cingulate (Elliott *et al*. 2002). In addition to cognitive-emotional processing, the ACC is involved in spatial planning and working memory, with depressed individuals demonstrating lower activation of this region than non-depressed controls while performing the Tower of London task (Elliott *et al*. 1997). Structural changes include bilateral volume reductions of the ACC in geriatric depression (Ballmaier *et al*. 2004), and a more specific finding of smaller left subgenual ACC volumes in non-geriatric depressed subjects (Hastings *et al*. 2004). Functional imaging studies have identified decreased metabolism and cerebral blood flow in the subgenual ACC of depressed individuals (Drevets *et al*. 2002; London *et al*. 2004).

A major cognitive role of the dorsolateral prefrontal cortex (DLPFC) is to subserve the implementation of attentional control. Mood-disordered individuals have demonstrated reduced left cingulate activation and increased left DLPFC activation for both affective and non-affective tests of response inhibition (the Stroop test) relative to non-depressed controls (George *et al*. 1997). Depressed individuals also evidence increased neural response in the DLPFC to an affective go/no-go task than non-depressed controls, which is presumed again to reflect an affective processing bias (Elliott *et al*. 2002). Although the DLPFC is not the primary substrate of cognitive-emotional processing, it is involved in several higher-order cognitive functions, including working memory (Owen *et al*. 1999), retrieval of episodic memory (Rugg *et al*. 1999), planning (Dagher *et al*. 1999), and response monitoring (Blakemore *et al*. 1998). On planning tests such as Tower of London-type tasks (e.g. CANTAB Stockings of Cambridge), depressed individuals demonstrate reduced perfusion in the right middle frontal cortex and left superior frontal gyrus relative to non-depressed individuals (Goethals *et al*. 2005). The cognitive findings of the

DLPFC in depression are consistent with the finding that depressed individuals demonstrate reduced metabolism in DLPFC relative to non-depressed individuals (Biver *et al*. 1994; Michael *et al*. 2003). Geriatric depression is associated with microstructural differences in the white matter of the DLPFC (Taylor *et al*. 2004) and reduced volumes of the superior and middle frontal cortices (Ballmaier *et al*. 2004), which may play a particularly important role in late-onset depression.

The hippocampus plays a complex role in affective regulation and a vital role in learning and recall. Cognitively, depressed elderly individuals demonstrate reduced hippocampal volume in association with lower levels of performance on tests of both verbal and visual episodic memory, which is seen in both early and late-onset depression (Hickie *et al*. 2005). Although the hippocampus is most frequently associated with episodic memory (Moscovitch *et al*. 2005), it may also regulate emotional responses to environmental stimuli (Phillips *et al*. 2003). Imaging studies of the hippocampus in depression are mixed; some studies have found decreased volume to be associated with depression among adults (Sheline *et al*. 1996; Frodl *et al*. 2004), while others have not (Hastings *et al*. 2004). Reductions in hippocampal volume are more consistently found among individuals with recurrent depression (MacQueen *et al*. 2003; Sheline *et al*. 2003), earlier age-of-depression onset (Sheline *et al*. 1999; MacQueen *et al*. 2003), and longer duration of untreated depression (Sheline *et al*. 2003). Smaller hippocampal volume has been associated with subsequent cognitive decline in older patients with depression (Steffens *et al*. 2002; O'Brien *et al*. 2004).

Vascular pathology and vascular depression

The preceding review of the cognitive neuroscience of depression highlights the crucial relationships between mood and structural changes in the aging brain. There are well-established associations between cerebrovascular pathology and development of depression in the elderly. Studies using magnetic resonance imaging (MRI) have suggested that subcortical ischemic changes may play a role in the pathology of geriatric depression, particularly in patients with late age of onset (Krishnan *et al*. 1988; Coffey *et al*. 1989; Figiel *et al*. 1991; Salloway *et al*. 1996; Kumar *et al*. 1999; de Groot *et al*. 2000). These findings led to the characterization of MRI-defined vascular depression (Krishnan *et al*. 1997; Steffens & Krishnan, 1998). Relative to depressed individuals without marked cerebrovascular pathology, individuals with vascular depression tend to be older, have higher levels of hypertension and other cerebrovascular risk factors, and less family history of depression (Krishnan *et al*. 2004; Taylor *et al*. 2006). The contribution of underlying cerebrovascular risk factors (CVRFs) to depression and cognitive impairment in general is indicated in a study that found that individuals with two or more CVRFs (diabetes, hypertension or atrial fibrillation) and lower scores on a measure of initiation and perseveration had significantly higher levels of depressive symptomatology at baseline and 18 months than individuals with fewer CVRFs and better cognitive performance (Mast *et al*. 2004). These data suggest that individuals with higher levels of CVRF and lower executive function performances are at greater risk of developing depression, possibly as a result of structural brain changes. The influence of structural brain changes is supported by findings that depressed elders with greater prevalence of deep-white matter hyperintensities (DWMHs) demonstrate worse performance on tests of memory and executive functions than either depressed elders or normal controls without DWMHs (Kramer-Ginsberg *et al*. 1999). The characterization of cerebrovascular pathology in depression is an important area of continued research not only because it may result in an acquired and persistent dysfunction in affect and cognition but also because of its association with slowed treatment response (Hickie *et al*. 1995; Simpson *et al*. 1997; Steffens *et al*. 2001, 2005), increased hospitalization (Yanai *et al*. 1998), greater functional impairment (Steffens *et al*. 2002), and increased mortality (Levy *et al*. 2003).

Depression and mild cognitive impairment (MCI)

Detection of MCI is a key clinical issue in depression because it is associated with accelerated cognitive decline and possible conversion to dementia. It is important to clarify that MCI is not a formal diagnostic entity, but rather is frequently used to characterize a state of non-normal cognitive function that is not severe or pervasive enough to meet formal diagnostic criteria for dementia. We use the term MCI in this section to describe non-normal cognitive function not meeting criteria for dementia, but note that other terminologies such as cognitively impaired, not demented (CIND) provide a similar characterization. Reported co-morbid prevalence of depression and MCI ranges from approximately 25% to 50% (Lopez *et al*. 2003*b*; Adler *et al*. 2004; Lee *et al*. 2007), which is much greater than the 3–6% prevalence of amnestic MCI in studies of community samples (Lopez *et al*. 2003*b*; Ganguli *et al*. 2004). Research indicates that MCI or other clinically significant cognitive impairment evolving during an episode of depression may persist after the depression episode has remitted (Reischies & Neu, 2000; Lee *et al*. 2007). Although not using a

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specific MCI classification, other studies have found that the extent of cognitive impairment in depressed older adults prior to treatment is associated with persisting cognitive impairment after treatment (Butters *et al*. 2000; Adler *et al*. 2004), particularly in the areas of processing speed and executive function (Nebes *et al*. 2003; Murphy & Alexopoulos, 2004). Persistent cognitive deficits in the context of depression are a significant clinical concern because they may reflect underlying structural changes that increase an individual's risk of converting to Alzheimer's disease (Butters *et al*. 2000) or another form of dementia.

Depression and dementia

Depression symptoms are a prominent clinical feature within a number of progressive dementing illnesses. The most common form of dementia is Alzheimer's disease (AD), and most studies report that 30–50% individuals with AD experience symptoms of depression, including low mood, apathy, social withdrawal and suicidal ideation (Zubenko *et al*. 2003). Major depression is common among patients with mild (11.5%) and moderate (10%) AD, but occurs at a lower rate in severe AD (4.5%) (Lopez *et al*. 2003*a*). Table 1 provides a comparison of major depression and the criteria for depression of AD. Depression symptoms are also common in patients with other forms of dementia, including vascular dementia (Sultzer *et al*. 1993; Park *et al*. 2007), dementia with Lewy bodies (Klatka *et al*. 1996; Papka *et al*. 1998; Ballard *et al*. 1999), Parkinson's disease (Tandberg *et al*. 1996; Weintraub & Stern, 2005) and Huntington's disease (Folstein *et al*. 1983).

The close relationship of depression to many conditions causing dementia raises the question of why this relationship exists, and to what extent may different etiologies account for depression occurring before *versus* after the onset of dementia. One point of debate centers on whether depression is a risk factor or prodrome of dementia. Several studies have found that remote histories of depression (10–25 years before onset of dementia) do increase the risk of later diagnosis of dementia (Broe *et al*. 1990; Steffens *et al*. 1997; Green *et al*. 2003). While these studies do suggest that a prior history of depression increases dementia risk, the magnitude of risk ratios decreases with increasing time between depression onset and dementia diagnosis (Broe *et al*. 1990; Steffens *et al*. 1997; Green *et al*. 2003), which makes it more likely in these cases that later age of onset of depression may be either a prodromal symptom or a susceptibility factor for later dementia. Evidence suggesting that depression presents as a prodrome of dementia comes from a longitudinal, population-based study of dementia, which found that depression symptoms increased after onset of dementia, but that prior depression alone did not increase dementia risk (Chen *et al*. 1999).

The question of whether dementia is a risk factor or prodrome of dementia does raise controversy, and there are putative biological explanations on both sides of the debate. For instance, hippocampal atrophy is associated with both depression and dementia, and studies have found that greater hippocampal atrophy is associated with both longer duration of depressive episodes (Sheline *et al*. 1999) and more recurrent depression (Shah *et al*. 1998). This would suggest that recurrent and chronic depression contribute to a degree of hippocampal atrophy that raises an individual's risk for later development of dementia, and there is neuropsychological evidence that individuals with chronic early onset of depression have greater relative deficits in hippocampally mediated processes of episodic memory than individuals with later onset of depression (Rapp *et al*. 2005). One explanation that has been posited for the adverse effects of chronic depression on the hippocampus is that stress-related hypercortisolemia occurring during depression has a toxic effect on the hippocampus and disrupts regulation of glucocorticoid secretion, which results in a cascade effect of hippocampal atrophy leading to cognitive impairment and ultimately dementia. Although support for this hypothesis exists among non-depressed individuals (Lupien *et al*. 1999), the evidence is mixed in studies of depression (Mitchell & Dening, 1996; Adler & Jajcevic, 2001), and there also does not seem to be strong evidence that the observed relationship between depression and hippocampal atrophy is related to cortisol levels (O'Brien *et al*. 2004).

Another possible explanation for the presence of depression in dementias such as AD may be related to loss of monoaminergic neurons in this disease (Lyness *et al*. 2003). A third hypothesis is that depression exacerbates pre-existing cognitive impairment by depleting cognitive reserve or otherwise lowering the threshold for clinical manifestation of dementia (Jorm, 2001). Other operational definitions based on neuropathology or rate of cognitive decline associated with depression history remain to be studied. In our view, the ideas of depression as a risk factor or prodrome of dementia are not mutually exclusive, but rather reflect the heterogeneous presentations and etiologies of both conditions. The more important scientific issues are identifying factors that cause depression to become a risk factor for dementia and determining factors that cause depression to emerge in prodromal dementia.

Table 1. *Comparison of major depressive episode and provisional criteria of depression of Alzheimer's disease (AD)*

Major depressive episode	Depression of AD
A. Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning	A. Three (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning: at least one of the symptoms is either (1) depressed mood or (2) decreased positive affect or pleasure
Do not include symptoms that are clearly due to a general medical condition, or mood-incongruent delusions or hallucinations	Do not include symptoms that, in your judgment, are clearly due to a medical condition other than Alzheimer's disease, or are a direct result of non-mood-related dementia symptoms (e.g. loss of weight due to difficulties with food intake)
(1) Depressed mood most of the day, nearly every day, as either indicated by subjective report or observation of others (2) Markedly diminished interest or pleasure in all, or almost all, activities most the day, nearly every day (either 1 or 2 are required) (3) Significant weight loss when not dieting, or weight gain, or decrease or increase in appetite nearly every day (4) Insomnia or hypersomnia nearly every day (5) Psychomotor agitation or retardation nearly every day (6) Fatigue or loss of energy nearly every day (7) Feelings of worthlessness or excessive or inappropriate guilt nearly every day (8) Diminished ability to think or concentrate (9) Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide	(1) Clinically significant depressed mood (e.g. depressed, sad, hopeless, discouraged, tearful) (2) Decreased positive affect or pleasure in response to social contacts and usual activities (3) Social isolation or withdrawal (4) Disruption in appetite (5) Disruption in sleep (6) Psychomotor changes (e.g. agitation or retardation) (7) Irritability (8) Fatigue or loss of energy (9) Feelings of worthlessness, hopelessness, or excessive or inappropriate guilt (10) Recurrent thoughts of death, suicidal ideation, plan or attempt
A. Does not meet criteria for a mixed episode. The symptoms are not better accounted for by bereavement B. The symptoms are not due to the direct physiological effects of a substance (e.g. a drug of abuse or a medication), or a general medical condition (e.g. hypothyroidism) C. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning	A. All criteria are met for dementia of the Alzheimer type (DSM-IV-TR) B. The symptoms cause clinically significant distress or disruption in functioning C. The symptoms do not occur exclusively during the course of a delirium D. The symptoms are not due to the direct physiological effects of a substance (e.g. a drug of abuse or a medication) E. The symptoms are not better accounted for by other conditions such as major depressive disorder, bipolar disorder, bereavement, schizophrenia, schizo-affective disorder, psychosis of Alzheimer's disease, anxiety disorders, or substance-related disorder

Adapted from Olin *et al.* (2002*a*, *b*). Also appears in Potter & Steffens (2007).

Assessment of cognitive impairment in late-life depression

Regardless of whether depression is a risk or prodrome of dementia, the important clinical issue is that the depression tends to co-occur with cognitive impairment, particularly in late life, which highlights the importance of assessing cognitive impairment as part of a long-term approach to managing depression. Although the assessment of cognitive impairment in late-life depression is predicated on an accurate assessment of depression itself, we focus in this review on the research addressing: (1) clinical differences between major depression and depression in AD and (2) brief *versus* comprehensive cognitive evaluation in older depressed adults. We assume that the reader is

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likely to be familiar with the need to rule out medical factors (e.g. sleep apnea, hypothyroidism) and medications (e.g. steroids, beta blockers) that can produce either cognitive impairment or behavioral and physical symptoms similar to depression (Patten & Love, 1994; Houston & Bondi, 2005).

Clinical characteristics of major depression and depression in AD

The constellation of depression symptoms presented by a patient provides information about whether these may reflect a dementia prodrome. A set of useful clinical features are provided by Olin *et al*. (2002*a*): (1) depressed individuals with cognitive impairment are more like to have a fully diagnosable episode of major depression, whereas depression in AD is typically less severe; (2) depression presents with higher levels of subjective cognitive complaint than in AD; (3) depression presents with a more rapid and mood-congruent onset of cognitive impairment, whereas cognitive impairment in AD following the slower, more progressive course that is typical of this disease; (4) cognitive impairment in depression is most strongly associated with effortful tasks, whereas cognitive impairment in the domains of language, gnostic processes and praxis are more likely to be seen in AD. A depressive syndrome in AD may present with fewer and less prominent symptoms than a primary diagnosis of major depression, with prominent features of social withdrawal and irritability (Olin *et al*. 2002*a*; Zubenko *et al*. 2003). Evidence also suggests that motivational deficits such as apathy are a better predictor of conversion to dementia than somatic or mood-related symptoms (Bartolini *et al*. 2005), and hence may be an important clinical characteristic of an emergent dementia prodrome. In fact, some have argued that apathy is distinct from depression in several neurological conditions (Levy *et al*. 1998), including a study that found that 13% of AD patients were positive for apathy in the absence of depression (Starkstein *et al*. 2001). Finally, mood-related symptoms in AD may decrease as cognitive impairment progresses, whereas somatic complaints may increase (Gilley *et al*. 2004).

Brief versus *comprehensive assessment of cognitive impairment in depression*

One important aspect of the clinical assessment of cognitive impairment in depression should be identifying cognitive screening instruments that differentiate the cognitive deficits most characteristic of depression from those that are most likely to reflect dementia. Unfortunately, there are few empirical data on screening measures that effectively discriminate between the cognitive presentations of dementia and depression. In a study that illustrates the diagnostic problem, the Short Cognitive Evaluation Battery was found to demonstrate 94% sensitivity and 85% specificity for discriminating AD from non-demented and non-depressed controls, but there was only 63% sensitivity with 96% specificity discriminating AD from individuals with depression symptoms (Robert *et al*. 2003). Another study found that a screening test based on cued recall had 83% sensitivity and 85% specificity in discriminating individuals with AD from individuals with depression, but that this declined to 58% sensitivity and 85% specificity in discriminating MCI from depression, which was interpreted to reflect the greater heterogeneity in MCI (Dierckx *et al*. 2007). Similar issues of test insensitivity in discriminating depression are present in the Mini-Mental State Examination (MMSE; Folstein *et al*. 2001), which is widely used to estimate the severity of cognitive impairment, but which is less sensitive to milder cognitive impairment that might be expected in depression because of a low ceiling of difficulty, narrow range of cognitive abilities assessed, and differential sensitivity to age, education and ethnicity (Tombaugh & McIntyre, 1992). Moreover, validity of the MMSE is reduced in psychiatric samples (Faustman *et al*. 1990), and there is limited assessment of the types of executive function deficits that characterize cognitive impairment in depression. Based on current evidence, there are no screening measures that are sufficiently valid for distinguishing among depression, MCI and dementia in a clinical setting, and this is even more of an issue when depression and cognitive impairment occur together. Currently, brief cognitive screening measures are most informative as complementary aspects of a thorough clinical assessment (Duff *et al*. 2002; Robert *et al*. 2003), and the presence of impairment on such measures may warrant a more comprehensive evaluation. Table 2 summarizes clinical and cognitive presentations in typical cases of major depression and AD.

In the absence of effective screening instruments to differentiate the cognitive presentations of depression and dementia, neuropsychological assessment remains an important diagnostic tool for characterizing the cognitive profile of depressed individuals. Research has long indicated that sensitivity and specificity for differential diagnosis of conditions such as dementia and depression are improved when multiple cognitive measures are used (Chaves & Izquierdo, 1992), and there are three important ways in which a neuropsychological assessment can inform diagnosis and treatment planning for depressed patients with cognitive impairment. First, comprehensive neuropsychological assessment can characterize a cognitive

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Table 2. *Typical clinical and cognitive presentations of major depression* (*MD*) versus *Alzheimer's disease* (*AD*)

Feature	MD	AD
Diagnosis	Major depression	Symptoms less severe and pervasive than MD
Age of onset	Above or below age 60	Uncommon below age 60
Rate and course of cognitive change	Acute; mood congruent fluctuations in cognition; can improve with remission, though deficits may persist	Insidious; progressive cognitive decline
Subjective memory complaints	Overestimate level of cognitive impairment	Underestimate level of cognitive impairment
Affect	Sadness equal to or greater than apathy	Apathy greater than sadness when mood changes are present; apathy may also exist without depression
Sleep–wake cycle	Often disturbed	Variable
Memory	Initial suppression of learning curve; improvement with repeated exposure	Flat learning curve despite repeated exposure
	Recall improves with retrieval cues	Rapid forgetting; cueing does not help recall performance
	Intrusion of previously learned information is atypical	Intrusion of previously learned information in attempted recall of new material
Aphasia/apraxia/agnosia	Uncommon	Emergence following memory impairment
Executive functions	Ranges from suppressed to impaired	May be compromised with co-morbid depression; otherwise decline occurs later in disease progression
Information processing speed	Slowed	Normal in early stage of disease
Psychomotor speed	Slowed	Normal in early stage of disease
Effort	Decreases with cognitive demand; disproportionate impairment on effortful cognitive tasks; 'don't know' responses	Normal effort; proportionate effort in response to cognitive demands

profile aiding differential diagnosis; for instance, whether an individual presents with frontally mediated deficits in memory retrieval and complex information processing that characterize a cognitive syndrome of depression or with hippocampally mediated deficits in memory storage and additional deficits in language or praxis that characterize AD (Butters *et al*. 1994). Second, neuropsychological assessment can also identify areas of cognitive impairment, such as memory or problem solving, that may play a role in cognitive or behavioral interventions (e.g. Alexopoulos *et al*. 2003, as discussed later), or executive function deficits that indicate a higher likelihood of functional impairment (Kiosses *et al*. 2001). Third, neuropsychological assessment is important in effectively tracking the extent to which cognitive deficits are either partially to fully reversible (as in depression and some medical conditions), stable (as in cerebrovascular event), or progressive (as in AD or other dementias).

Pharmacological management of cognitive impairment in late-life depression

In general, a clinician does not start pharmacological treatment specific for cognitive symptoms in acutely depressed patients when cognitive impairment is consistent with their depressive disorder. Furthermore, starting both an antidepressant medication and a cognitive medication will complicate the clinician's ability to manage side-effects and adverse events, particularly gastrointestinal complaints. The exception to this approach is when co-morbid dementia is suspected, though not confirmed, in an older depressed patient, in which case treatment with a cholinesterase inhibitor (e.g. donepezil, galantamine, rivastigmine) or an *N*-methyl-D-aspartic acid (NMDA) receptor antagonist (memantine) may be warranted, depending on the severity of the dementia. Nonetheless, many clinicians prefer a stepwise approach to treatment, choosing to initiate an antidepressant and achieve

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a therapeutic dose prior to adding an anti-dementia agent.

Even when clinicians may not immediately treat cognitive impairment in the context of geriatric depression, it is important to recognize that the presence of cognitive impairment can adversely influence the patient's response to treatment. Behaviors such as perseveration and decreased initiation are among the types of executive function deficits that are associated with lower acute response rates to pharmacological treatment (Kalayam & Alexopoulos, 1999; Potter *et al*. 2004) and also predict a higher likelihood of recurrent depression over a 2-year period (Alexopoulos *et al*. 2000). However, executive dysfunction has not been found to be related to recurrent depression in all studies (Butters *et al*. 2004). Thus, depression and executive dysfunction may be independent among some individuals, but in others, the combination of executive dysfunction and persistent depression may reflect a common underlying dysfunction in the frontostriatal system. Nonetheless, the key point is that the presence of cognitive impairment may complicate management of depression in the older adult, and will necessitate more active monitoring of patient response.

Non-pharmacological intervention for depression and cognitive impairment

One reason that psychotherapy is an important component of depression treatment is that the combination of antidepressant medication and treatments, such as cognitive-behavioral therapy and interpersonal therapy, often produce better symptom improvement and maintenance of response than either psychotherapy or pharmacotherapy alone (Keller *et al*. 2000; Lenze *et al*. 2002; Lynch *et al*. 2007). Non-pharmacological interventions are also important in treating geriatric depression because many individuals either do not respond to medications or discontinue them due to adverse side-effects (Lyketsos *et al*. 2002). These outcomes may be more common in older depressed adults with cognitive impairment, and suggest that specific approaches to psychotherapy may mitigate some cognitive deficits associated with depression. One study found a 12-week trial of problem-solving therapy to be associated with higher remission rates and lower functional disability compared with supportive therapy when implemented in depressed older adults with demonstrated deficits in executive functions (Alexopoulos *et al*. 2003). In this case, the key therapeutic agent appeared to be the focus on practical problem-solving strategies, which would be beneficial to individuals whose perseverative thinking and other deficits in executive functions might otherwise inhibit effective coping and problem solving.

Conclusions

The purpose of the current review was to highlight key theoretical and clinical issues surrounding the presence of cognitive impairment in geriatric depression within the framework of current research. Cognitive impairment is common in depression among older adults, and the combination of these two conditions raises the risk for a number of adverse outcomes. Cognitive impairment occurring as a result of depression often complicates treatment, which may lead to persisting 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 therapeutic interventions.

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Declaration of Interest

None.

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