Late-life depression with comorbid cognitive impairment and disability: nonpharmacological interventions

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Abstract: Less than half of older adults with depression achieve remission with antidepressant medications, and rates of remission are even poorer for those with comorbid conditions. Psychosocial interventions have been effective in treating geriatric depression, either alone or better yet, in combination with antidepressant medications. Traditional strategies for nonpharmacological treatment of late-life depression do not specifically address the co-occurring cognitive impairment and disability that is prevalent in this population. Newer therapies are recognizing the need to simultaneously direct treatment efforts in late-life depression towards the triad of depressive symptoms, cognitive dysfunction, and functional disability that is so often found in geriatric depression, and this comprehensive approach holds promise for improved treatment outcomes.

Keywords: geriatric depression, dementia, functional impairment, psychotherapy

Introduction
Depression is a devastating illness for patients and their families. Although efficacious treatments for late-life major depression are available,1,2 depression in older adults is underdiagnosed and undertreated,3–5 particularly in primary care settings.6,7 Although the treatment of late-life depression with antidepressant medication appears to be increasing, disparities exist regarding who receives such treatment.8 When treated with pharmacotherapy alone, fewer than half of older adults with major depression achieve remission.9–12 Rates of remission are even lower in cognitively impaired, disabled older adults, where these comorbid issues complicate treatment adherence and other elements essential to success. As a result, psychosocial interventions are particularly important for the treatment of depressed older adults with comorbid cognitive impairment (CI) and disability. This review will address the complex relationship of depression, CI, and disability and will provide an overview of currently available psychosocial interventions for geriatric depression, with attention to promising therapies that incorporate more comprehensive approaches for the most vulnerable depressed, cognitively impaired, disabled elders.

The triad of late-life depression, CI, and disability
Maturational changes in the brain may increase vulnerability for the development of late-life depression13 and have etiological significance for declines in cognition and daily functional skills. Cerebrovascular changes, whether due to aging or disease, can compromise the neural connectivity of frontal systems. These alterations, including
connections with the limbic system, have been hypothesized to increase vulnerability for depression and contribute to the manifestation of executive dysfunction associated with late-life depression.\textsuperscript{9,14} Vascular insults need not be large to affect these neural systems. Large-scale epidemiological studies have found evidence that otherwise asymptomatic white matter changes on neuroimaging are associated with mild CI in older adults.\textsuperscript{15–17} Cognitive compromise and disability can foster nonadherence and interfere with treatment efforts in depressed older adults. Additional evidence suggests that CI is associated with poor and slower response to antidepressant medications.\textsuperscript{9,18,19}

**CI in late-life depression**

Cognitive compromise associated with late-life depression can present anywhere along a continuum from mild CI to a frank dementia. A mood disturbance in an older adult can initially present as subjective cognitive complaints. Likewise, the existence of depression can exacerbate previously existing cognitive difficulties. In community-dwelling residents, the combination of impaired cognition and depressive symptoms doubles in frequency at 5-year intervals beyond age 70; combined depression and cognitive dysfunction are present in 25% of individuals aged 85 years or older.\textsuperscript{20} There is ample evidence that the presence of comorbid cognitive deficits is associated with reduced treatment responsiveness in late-life depression.\textsuperscript{18,21–24}

The relationship of late-life depression and CI is complex. Late-life depression often is accompanied by executive dysfunction, which manifests as reduced planning, initiation, organization, and sequencing.\textsuperscript{25–27} Cognition can be affected in terms of new learning,\textsuperscript{28} visuospatial skills,\textsuperscript{29,30} and reduced psychomotor speed.\textsuperscript{31} Cognitive deficits may persist in depressed older adults even after depression remits.\textsuperscript{32–34} The presence of a dementing disorder in and of itself can increase the risk of depression.\textsuperscript{35} Conversely, the presence of depressive symptoms in cognitively intact older adults predicts subsequent cognitive decline.\textsuperscript{36} There is evidence that training in speed-of-processing skills is associated with less incidence of depression at follow-up,\textsuperscript{37,38} improved health-related quality of life,\textsuperscript{39} and self-rated health,\textsuperscript{40} whereas training in reasoning skills is associated with improved ability to perform instrumental activities of daily living.\textsuperscript{41}

Research has noted cognitive differences between early-onset and late-onset late-life depression. Individuals with late-onset depression (ie, first depressive episode occurring at 60 years or older) exhibit more impairment in overall cognitive deficits and in memory and executive dysfunction than those with early-onset depression.\textsuperscript{35,42,43} Furthermore, late age of depression onset is associated with the development of dementia in nondemented depressed older adults.\textsuperscript{44}

**Disability in late-life depression**

The World Health Organization conceptualizes disability as an overarching term that contains three types of dysfunction: compromised body function or structure, impairment in activity, and cessation in participation.\textsuperscript{35} In most studies, disability or functional impairment is concerned with problems in any one or all three of these areas. The relationship of depression and disability is bidirectional with empirical evidence suggesting that late-life depression promotes disability, and likewise, disability increases the risk of depression.\textsuperscript{46} Depression leaves older adults vulnerable to disability regardless of the presence of medical illness.\textsuperscript{47–50} In those who are already medically compromised, depression can increase the chances of disability, independent of the severity of the medical illness.\textsuperscript{49} This predisposition toward depression is evident in older psychiatric patients,\textsuperscript{49,51–53} medical inpatients,\textsuperscript{54} primary care patients,\textsuperscript{55} and older community-dwelling residents.\textsuperscript{56} The course of disability parallels the course of depression in that disability scores improve as a reflection of improvement in depression over time.\textsuperscript{57,58} Studies have not found significant differences between early-onset and late-onset depression in terms of disability.\textsuperscript{42,43} Although depression promotes disability, clinical intuition and empirical evidence argue that the reverse is also true; disability fosters depression.

Depression is projected to be the second leading cause of disability worldwide by 2020.\textsuperscript{39} Disability resulting from medical or neurological illnesses is associated with increased risk for a first-onset depressive disorder.\textsuperscript{47,60} In addition to factors such as bereavement, sleep disturbances, and prior depression, disability is an important risk factor for depression in older adults.\textsuperscript{61} In homebound elders, chronic and new-onset functional impairment are associated with increased risk for depression.\textsuperscript{49} Disability in the form of an increased risk of falls is associated with depression in later life.\textsuperscript{62,63} Severity of depression, degree of CI, and medical burden explain less than 40% of the variance in disability, implying that disability is a broader dimension of health status than each of these factors alone.\textsuperscript{51}

The relationship of depression and disability becomes even more complex in the presence of CI. On the one hand, the effect of late-life depression on disability may be
independent of concomitant changes in cognitive status. On the other hand, depression may contribute to disability in part due to the CI that often accompanies late-life depression. CI contributes to disability in late-life depression even after controlling for the effects of severity of depression. Deficits in executive functioning (e.g., planning, organizing, initiating, and shifting) are independently associated with impairment in instrumental activities of daily living, such as bill paying, doing housework, and taking medication in both demented and nondemented elders. Furthermore, cognitive deficits have the greatest effect on daily functioning in nursing home residents even after controlling for psychiatric symptoms of depression, delusions, and behavioral disturbances. There is also evidence that cognitive deficits, particularly impairments in problem solving and memory, mediate the effect of depression on disability.

**Limited efficacy of antidepressant medication in depressed, cognitively impaired, older adults**

Despite evidence that pharmacotherapy is efficacious in the acute treatment of late-life depression, this is not the case for those older adults with CI. Antidepressant medications bring to remission fewer than 40% of elderly depressed patients who have some degree of CI. Cognitive deficits, in particular measures of executive dysfunction such as reduced information processing speed, have been associated with slow and/or poor response to antidepressant treatment in this population.

**The effects of the triad on patients and caregivers**

Depression, CI, and disability contribute to increased medical and psychiatric morbidity and mortality. This triad also contributes to patient suffering, decreased quality of life, impairment in social and interpersonal functioning, and even leads to early nursing home placement. Caregivers of these individuals suffer similar consequences, such as decreased quality of life, medical and psychiatric morbidities, as well as increased risk of mortality. Similarly, caregivers of nondemented cognitively impaired older adults report increased burden and psychiatric morbidity. Family caregivers of depressed older adults without CI experience burden to a similar degree as caregivers of dementia patients. As a result, late-life depression has deleterious consequences not only for depressed older adults but also for those who provide direct care to these individuals.

**Psychosocial interventions in late-life depression**

Health care policy restructuring is placing greater demands on the use of treatment interventions that can be empirically supported. Using the criteria for evidence-based treatments set forth by the Committee on Science and Practice of the Society for Clinical Psychology (Division 12) of the American Psychological Association, several psychosocial interventions can be defined as evidence-based: behavioral therapy (BT), cognitive BT (CBT), cognitive bibliotherapy, problem-solving therapy (PST), brief psychodynamic therapy, and reminiscence therapy. Using more focused criteria, Mackin and Arean identified CBT (including PST), brief psychodynamic therapy, and to some extent reminiscence therapy as evidence-based interventions for late-life depression.

Although not without limitations, meta-analyses have been helpful in drawing conclusions on the current state of psychosocial interventions for late-life depression. Cuijpers et al analyzed 25 randomized studies and found that these treatments had a moderate to large mean effect size. This meta-analysis reported no significant differences in the effects among psychological interventions (i.e., CBT, BT, reminiscence therapy, interpersonal psychotherapy [IPT], PST, and others), no significant difference in effect of antidepressant medication vs psychological intervention, and a significantly larger effect of combined antidepressant and psychological intervention than antidepressant medication alone. In another meta-analysis that included nonrandomized studies but accounted for quality of study, Pinquart et al reported that CBT and reminiscence therapy had large effects, whereas most of the remaining psychosocial interventions had moderate effects.

**Cognitive behavioral therapy**

CBT in its various forms focuses on the interplay between thoughts, feelings, and behaviors. CBT emphasizes the identification of emotions and monitoring mood in relation to thoughts and behaviors. Cognitive aspects of the treatment involve identifying maladaptive and negative thinking patterns in depressed individuals, evaluating these thoughts in terms of their irrationality, and challenging and restructuring these thoughts in such a way as to be more adaptive and less depressive. Behavioral aspects of the treatment involve activating the patient via activity scheduling, evaluating patients’ expectations of their ability to accomplish tasks and activities successfully and/or to experience enjoyment in activities, and using positive reinforcement of desired...
behaviors.\textsuperscript{89-91} In the treatment of late-life depression, CBT has been significantly effective in reducing symptoms of depression when compared with a nontreatment control group.\textsuperscript{92-97} When compared with other active treatments, CBT was as good as other psychotherapies at treating depression,\textsuperscript{92,98-100} was superior or equivalent in maintaining treatment gains,\textsuperscript{98,101} and when used in combination with an antidepressant medication, was more effective in reducing depressive symptoms than either CBT or antidepressant treatment alone.\textsuperscript{102} More recent studies have continued to support CBT as an effective treatment.\textsuperscript{103,104}

**Problem-solving therapy**

Often considered a form of CBT, PST has garnered evidence as an effective treatment for late-life depression. PST consists of a structured format through which depressed older adults learn specific skills to enhance problem-solving abilities and, through successful resolution of problems, decrease depression. Problem-solving skills training consists of identifying and defining a problem, generating alternative solutions, analyzing positive and negative consequences of solutions, and carrying out a solution and subsequently evaluating the outcome.\textsuperscript{105} In depressed older adults, PST was superior to reminiscence therapy and a wait-list control group\textsuperscript{106} and was more effective than supportive therapy.\textsuperscript{35,107}

Studies comparing PST with treatment as usual in primary care\textsuperscript{108} and home care\textsuperscript{109,110} continue to support the usefulness of PST for depression in older adults.

**Reminiscence therapy**

Reminiscence therapy is a long-standing treatment modality that has been used to address depression in older adults. Based on Erikson’s psychosocial developmental theory reminiscence therapy emphasizes the review of life and identification of meaning and purpose in one’s life. This is done through a process of inspection of one’s life through memories, focusing on both positive and negative experiences, and developing perspective. Reminiscence therapy, with its emphasis on personal experiences and history, lends itself to the older adult context. Studies have found that reminiscence therapy has been more effective than nonpsychotherapy social services\textsuperscript{111} and nontreatment conditions.\textsuperscript{106,112-115} However, its effectiveness compared to other active interventions remains questionable.\textsuperscript{116,117}

**Brief psychodynamic therapy**

Psychodynamic therapy, particularly in its brief form, has empirical findings that support its effectiveness in treating late-life depression. Brief psychodynamic therapy focuses on the identification of conflicts and unconscious processes, often originating from early developmental stages. Brief psychodynamic therapy encourages the development of insight and gives importance to the relationship and interactions of the therapist and client. As with other psychotherapies, more research is required to determine brief psychodynamic therapy’s robustness as a treatment (eg, in comparison to or combination with antidepressant medication).

**Interpersonal psychotherapy**

Another intervention often cited in the late-life depression literature is IPT. IPT focuses on interpersonal problems in four areas: role transitions, interpersonal role conflicts, grief, and interpersonal skills deficits.\textsuperscript{118} IPT appears to have clinical utility in treating late-life depression\textsuperscript{119} and potential in combination with antidepressant medication.\textsuperscript{120} More recent analyses have indicated that maintenance IPT is not as effective as supportive clinical management in sustaining gains made in health-related quality of life,\textsuperscript{121} but it may lower the risk of recurrence of major depression in older adults who have lower cognitive functioning.\textsuperscript{122} Although it remains a promising treatment for depression in later life, IPT continues to lack the empirical requisites for addition to the evidence-based intervention listing.\textsuperscript{86,123}

**Need for tailored nonpharmacological interventions for late-life depression**

Most psychosocial interventions for the acute treatment of geriatric major depression focus on “young–old” (average age of 65–70 years), cognitively intact, ambulatory older adults who can follow outpatient treatment.\textsuperscript{86} Clearly, this is only a subsample of the population who are in need. Homebound, rural, and low-income older adults may not have the same access to effective interventions for depression as those living in situations more conducive to receiving traditional psychotherapeutic treatment.\textsuperscript{38} Furthermore, interventions may not be available or appropriate for ethnically and culturally diverse populations. Factors such as comorbid illness can also serve as a barrier for treatment. Evidence suggests that depressed older adults with comorbid physical illness and CI experience reduced intervention effectiveness,\textsuperscript{88} which argues for a strong need for new evidence-based psychosocial interventions to help depressed older adults with CI and disability. Studies have not indicated significant treatment remission differences between early-onset and
late-onset depression,124 although older adults who had an early-onset depression may be slower to remit.125

Targeting the triad
A small number of studies have started to address the triad of late-life depression, CI, and disability. These are adaptations of the traditional forms of psychosocial therapies for late-life depression that accommodate CI and disability, both by what is targeted in treatment and by how treatment is executed. Another important adaptation is the inclusion of family members and caregivers in the treatment.

Psychosocial interventions for depressed older adults with mild cognitive deficits
Two interventions have been successfully adapted for depression in older adults with mild CI: PST35,107 and IPT.126 PST was adapted for depressed older adults with mild executive dysfunction, and recent data suggest that it is efficacious in reducing depression and disability in this population.35,107 IPT was modified for depressed older adults with mild CI (IPT-CI) by including the systematic incorporation of concerned caregivers into the treatment process, with joint patient–caregiver sessions to promote better understanding, communication, and respect.126,127 In addition, IPT-CI helps both the older adult and his or her caregiver through their role transitions that result from cognitive deficits and functional limitations.

Psychosocial interventions for depressed, disabled older adults with moderate to severe cognitive dysfunction
In patients with more moderate to severe cognitive compromise, there can be a spectrum of neuropsychiatric features. These include depressive symptoms and other behavioral impairments that can be addressed by psychosocial interventions. The following psychosocial interventions have been proposed for the treatment of major depression in advanced CI, including dementia.

CBT for early stage dementia
CBT has been adapted for depressed older adults with mild stages of dementia, but no efficacy data are available.128 The CBT-mild dementia protocol is 16–20 sessions long and includes a comprehensive neuropsychological battery to assess the cognitive deficits and the cognitive strengths of the patient. The treatment consists of behavioral activation and the incorporation of memory aids (eg, notepads and audio taping of sessions), as well as the cognitive components of examination of the evidence for and against a specific condition, listing the pros and cons of situations, and experimenting with new attitudes and cognitions in stressful situations.128

Problem adaptation therapy
Problem adaptation therapy (PATH) is a relatively new 12-week home-delivered intervention specifically developed to treat late-life major depression presenting with significant CI (including mild to moderate dementia) and disability.129,130 PATH focuses on the patients’ ecosystem, which involves the patient, the caregiver, and the home environment. PATH utilizes PST as its basic framework to promote adaptive functioning and integrates environmental adaptation tools (PATH tools), including calendars, checklists, notepads, signs, and timers, to bypass the functional and behavioral limitations of these patients. Finally, willing and available caregivers participate in treatment when the patient cannot utilize problem-solving skills, employ environmental adaptations, and engage in pleasurable activities. Preliminary efficacy data suggest that PATH is effective compared with a control condition of home-delivered supportive therapy in reducing both depression and disability.129

Behavioral treatment for depression in moderate to severe dementia
A behavioral treatment developed by Teri et al131 focused on teaching caregivers strategies aimed at increasing patients’ pleasant events or aiding them with problem-solving skills. In a controlled clinical trial, this behavioral intervention was useful in reducing depressive symptoms in older adults with major or minor depression and moderate to severe dementia, with symptom reduction maintained at 6-month follow-up. Another finding of this study was that caregivers of those receiving behavioral interventions experienced significant reduction in depression compared with those in the control groups. This behavioral approach is the recommended intervention for older adults with depression who are in the more moderate to severe stages of dementia.

Conclusion
Clinicians should be aware of the complexities of geriatric depression and how problems with cognitive and physical functioning play a role in the presentation of depressive symptoms. Effective interventions for geriatric depression should recognize the older adult’s potential limitations in key areas of cognitive functioning, such as information processing, organization, and memory, that may impact
engagement in therapy and following through of treatment plans. Consideration of the individuals’ mobility and their ability to independently manage health behaviors and routines is essential to the success of the intervention. Treating depressive symptoms in isolation of the patients’ cognitive and physical limitations risks slower or less-effective reduction in depressive symptoms; however, targeting the triad of depression, CI, and disability provides a concerted effort to help patients adapt and cope up with their problems, promoting successful outcomes for depression treatment. Although evidence for such multi-faceted approaches to treatment is nascent, large-scale studies and further intervention development are currently underway. Given the high prevalence of depression in older adults, establishing more effective treatments is vital to improving geriatric mental health and quality of life for patients and their families.

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