

Depression vs. Dementia: How Do We Assess?

Depressive disorder and dementia are common in older people, and may occur separately or together. Diagnosis is often challenging because of the frequency of symptoms which are common to both disorders. Unfortunately, underdiagnosis of depression results in missed opportunities to improve functioning, decreased quality of life and possibly even increased mortality. Yet, overdiagnosis of depression may result in unnecessary adverse effects of psychotropic medications. This article suggests approaches to differential diagnosis.

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Dementia increases with age, with an overall prevalence in Canada of 8% in those 65 years and older, 2.4% in those aged 65 to 74 years, 11.1% in those aged 75 to 84 years, and 34.5% in those aged 85 years and older.¹ Alzheimer's disease (AD) is thought to be the most common type of dementia in all age groups. However, younger age groups are more likely than older age groups to be diagnosed with other dementias, such as frontotemporal dementia and vascular dementia.²

Major depressive disorder is also common, but is only one of a number of disorders listed in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)³ with prominent depressive symptoms (Table 1).³

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These include dysthymic disorder, depressive episodes of a bipolar disorder, mood disorders secondary to a medical disorder (such as hypothyroidism), mood disorders secondary to a substance, adjustment disorders and bereavement. Depressive disorder is commonly seen in all stages of adult life and, while its prevalence is slightly lower in the elderly,⁴ its sequelae are probably greater in more frail people, exerting a more deleterious effect on functional abilities and even increasing the length of stay for hospitalizations related to primary medical conditions.⁵ Depressive disorder in seniors can occur as part of a lifelong recurrent disorder, or it can present for the first time in old age. It is frequently concurrent with other medical and mental disorders, including various dementias.

Relationships Between Dementia and Depression

Dementia and depression have a complicated relationship, with at

least two contradictory directions of potentially causal influence. One hypothesis suggests that depression leads to dementia, and another that suggests that dementia itself leads to depression.

The depression-to-dementia direction is supported by evidence that depressive disorder is a risk factor for developing dementia in later life⁶ and, consistent with this, the best-studied people with a biological predisposition to develop AD (those with Down Syndrome) are thought to have a high risk of suffering from depression.⁷ The association between depression and later development of dementia is still not completely understood. One possibility is that depression is an early, prodromal phase of dementia,⁸ and is caused by the same pathophysiologic initiators that result in dementia. There is also evidence that depression is associated with damage to brain locations integral to cognitive processes, such as the hippocampus, possibly by decreasing neurogenesis.⁹ This

Table 1

DSM-IV Mental Disorders with Prominent Depressive Symptoms³

- Major depressive disorder
- Dysthymic disorder
- Bipolar disorder (depressive episode)
- Mood disorders secondary to a general medical condition
- Mood disorders secondary to a substance (such as a medication)
- Adjustment disorder with depressed mood
- Bereavement

process may lower the threshold for later observable cognitive loss, eventually increasing age-adjusted dementia rates. Behaviors associated with depression, such as heavy alcohol uses and vascular risk factors like cigarette smoking,¹⁰ may also independently increase later cognitive loss, while medications prescribed to treat depression, especially those with strong anticholinergic effects, could conceivably have adverse cognitive effects, although this effect is likely more transient.

The dementia-to-depression direction in the potentially causal relationship between the two disorders is supported by findings that people with dementia appear to have a higher prevalence of depression.¹¹ However, prevalence rates vary widely depending on the study population (psychiatric outpatients, Alzheimer registries, old-age homes), instruments used, and diagnostic definitions. Most problematically, the term depression is used to denote different clinical concepts, which are not always equivalent to a diagnosis of DSM-IV major depressive disorder.

Muller-Thomsen et al¹² illustrated large variability in the diagnosis of

depression in dementia by using four different scales in the same population, and found that between 27.5% and 53.4% of people with mild AD and between 36.3% and 68.4% with moderate to severe AD were found to rate positive for depression. Studies comparing differences in the prevalence of carefully diagnosed depressive disorders between matched demented and non-demented populations are not frequent, but suggest that motivational deficits in dementia may be the greatest difference between these groups, rather than typical DSM-IV major depressive disorder.¹³ However, regardless of the exact prevalence of formally diagnosed depressive disorder in dementia, it does seem that depressive syndromes are very common in those with dementia, and that this comorbidity causes increased deficits in functioning, increased problematic behavior,¹¹ increased nursing-home placement,¹⁴ increased caregiver stress,¹⁵ and increased mortality.¹⁶

Under- and Overdiagnosis of Depression in Dementia

Depressive disorder has long been thought to be underdiagnosed in

those with dementia,^{17,18} although a recent Danish study suggests that this may now have changed, at least in Denmark.¹⁹ Underdiagnosis of depression in demented seniors is clearly undesirable, as depressive disorders in the demented elderly have been associated with additional burden, as described above. Undertreatment with antidepressants may also result in over treatment of depression-associated behaviors with benzodiazepines and possibly neuroleptics. Adverse effects of benzodiazepines and neuroleptics are well recognized and include increased falls, decreased alertness, extrapyramidal side effects, decreased mobility, decreased functioning and increased mortality. Efforts have been made to increase the recognition of depression in those with dementia, and widely used instruments such as the Minimum Data Set²⁰ include quality indicators to alert administrators of patients with likely depression who are not being treated with antidepressants. Review of these quality indicators may precipitate discussion with attending physicians, who have the opportunity to institute appropriate treatment.

Unfortunately, this process may also result in an overdiagnosis of depressive disorder due to the high prevalence of behavioral symptoms in dementia such as apathy and reactive mood symptoms, which overlap with those seen in major depressive disorder. Treatment with antidepressants is increasingly also known to be associated with adverse effects, most problematically in older, frail populations. Anticholinergic effects of the tricyclic antidepressants may cause confusion, constipation, urinary reten-

tion, and visual-accommodation problems. Postural hypotension may cause falls, and cardiac effects are particularly dangerous in overdose. Newer medications, such as selective serotonin reuptake inhibitors (SSRIs) and venlafaxine, were initially felt to be much safer, but have been increasingly associated with different, rather than fewer, adverse effects.

Gastrointestinal side effects and sleep disturbances appear to be more common with this group of medications. Recent research has suggested that SSRIs are no less likely than tricyclic antidepressants to cause falls.²¹ They are also associated with a higher prevalence of hyponatremia,²² and most recently research has suggested they increase fragility fractures.²³ Finally, SSRIs have been associated with increased apathy,²⁴ even in those who have been appropriately diagnosed with depression and have responded to this medication.

Challenges in the Diagnosis of Depression in Dementia

Diagnosing depressive disorder in the context of dementia is often difficult due to overlapping symptoms between depression and dementia, communication problems and lack of insight. Behavioral and psychological symptoms of dementia (BPSD) are integral parts of the clinical presentation of dementia, although this is often thought of as a disorder of progressive cognitive decline. BPSD includes many of those symptoms also seen characteristically in DSM-IV depressive disorders. Of the core symptoms of depressive disorder, listed in Table 2, sleep disturbances, changes in eat-

Table 2

DSM-IV Symptoms of a Major Depressive Episode

- Depressed mood
- Markedly diminished interest or pleasure
- Significant weight change
- Changes in sleep patterns
- Psychomotor agitation or retardation
- Fatigue or loss of energy
- Feelings of worthlessness, excessive or inappropriate guilt
- Diminished ability to think or concentrate
- Recurrent thoughts of death, suicidal ideation or suicidal actions

ing behavior, decreased initiative and interest (apathy), psychomotor agitation, and poor concentration (in advanced dementia) are common in dementia without depression. Reactive symptoms such as anxiety and tearfulness are also seen frequently in dementia without depression, and may be related to retained awareness of deficits in the early stages of dementia, poor coping skills and disorientation in the later stages, or to the mood lability accompanying vascular brain disease (which commonly overlaps with AD).

Much less common in dementia without depression are consistent sadness, marked morning mood worsening, feelings of worthlessness or excessive or inappropriate guilt, recurrent thoughts of death, suicidal ideation or suicidal actions.

Approach to Clinical Diagnosis

A variety of instruments have been developed to screen for depression in the cognitively intact population. These include the Beck Depression Inventory,²⁵ the Centre for Epidemiological Studies-Depression Sca-

le,²⁶ the Geriatric Depression Scale,²⁷ the Hamilton Depression Rating Scale,²⁸ the Montgomery and Asberg Depression Rating Scale²⁹ and the Zung scale.³⁰ Although these scales vary considerably in how much they are affected by impairments in language, awareness and comprehension, none is useful in the later stages of dementia. Of greater usefulness in patients with advanced dementia are the Dementia Mood Assessment Scale³¹ and the Cornell Scale for Depression in Dementia.³²

However, the gold-standard differential diagnosis of depression in dementia is a careful clinical assessment, which includes obtaining information directly from the patient and from collateral sources, ideally those with good knowledge of the person. This assessment should include:

- Careful symptom history including:
 - detailed description;
 - time course and progression of symptoms; as well as
 - association with other confounding factors such as environmental stressors which include:

Table 3

Typical Presentations of Mood Symptoms in Dementia and Depression

Symptom	Dementia	Depression
General response to cognitive and functional decline	Frequent lack of concern or denial about symptoms.	Amplification of and excessive preoccupation with deficits.
Mood	Normal most of the time. Unhappiness is reactive to circumstances and fluctuates. Labile, especially with vascular dementia. Mood often brightens with stimulation and support.	Subacute (weeks) onset of pervasively sad mood, most of the day and nearly every day. Doesn't brighten much with stimulation.
Interest, initiative	Gradual loss of interest and initiative (apathy) over a longer period of time (years rather than weeks). Not accompanied by statements of sadness, tearfulness, or other distress. Still enjoys activities in a structured environment.	Subacute loss of interest and pleasure over a few weeks, frequently accompanied by sad mood and affect, and occasionally statements of guilt, hopelessness and self-harm.
Eating behavior and weight	Gradual loss of weight (over months to years) which is common in dementia. Large increases in weight may be secondary to decreased activity, medications, and hyperorality in patients with frontal behavioral presentations (more common in frontotemporal dementia like Pick's Disease).	Subacute changes (weeks) in appetite leading to increase or decrease in weight.
Sleep	Gradual disruption of the sleep-wake cycle (over months to years) due to brain changes of dementia, resulting in frequent night-time waking and daytime sleeping.	Subacute changes in sleep over a few weeks (increase or decrease).
Psychomotor agitation	Gradual (months to years) increase in agitation, generally worse during the latter part of the day (sundowning). Patient much worse in unfamiliar settings (catastrophic reaction), and often seeking people or places from earlier life experiences.	Subacute (weeks) onset, often worse in the morning, may be present persistently throughout the day. Generally accompanied by other depressive symptoms such as nihilistic statements or excessive guilt.
Psychomotor retardation	Seen infrequently in mild to moderate dementia, but occasionally in very advanced dementia, and may be mimicked by Parkinson's dementia (facial masking, slow motor functioning) or advanced Pick's Disease.	Subacute onset of psychomotor retardation (over weeks) in severe depression.
Energy	Generally a normal energy level, but reduced activity due to poor initiation related to decreased executive functioning.	Subacute decrease in energy and increased complaints of fatigue.
Guilt or worthlessness	Uncommon, although transient statements of worthlessness might be seen in times of stress in those with preserved awareness of their own decline.	Common in severe depression, usually accompanied with low mood as well as changes in appetite and sleep.
Concentration and thinking	Concentration is normal in early dementia, but impaired in late dementia. Thinking ability declines throughout the course of dementia.	Subacute loss of concentration and sustained focus. Often indecisive and concerned about making mistakes.
Suicidal thoughts and actions	Uncommon.	Common.

- pain;
- poor nutritional status;
- other medical conditions; and
- recent changes in medications.
- Particular attention should be paid to depressive symptoms which are less common in dementia alone such as:
 - hopelessness;
 - expressions of guilt;
 - feelings of worthlessness; and
 - thoughts of self-harm.
- Frontal symptoms, such as disinhibition, perseveration and decreased initiative, suggest dementias with a strong frontal component rather than depression.
- Information about family history of mood disorders, previous personal history of depression and previous response to therapy for depression.
- Direct interview of the person, paying particular attention to:

consistently low mood and affect that does not respond to stimulation; hopelessness, expressions of guilt; feelings of worthlessness; and thoughts of self-harm.

- Laboratory investigations, such as hematology, thyroid function, electrolytes, vitamin B12, and drug levels of medications, known to have a propensity to cause mood symptoms.

In addition to the above, neuroimaging might be performed to explore the potential contribution of vascular pathology to mood lability and apathy, and to rule out other neurologic problems such as normal-pressure hydrocephalus.

After this assessment, the clinician has to weigh the information obtained, taking into account the likelihood that the accumulated information represents depression rather than dementia alone. For example, isolated symptoms of apa-

thy without associated sadness, crying, or changes in sleep or appetite are unlikely to represent a depressive disorder, whereas consistently sad mood or affect, not brightening during interpersonal contact and associated with subacute changes in sleep and appetite are much more likely to represent depressive disorder that requires medical treatment. Table 3 summarizes mood symptoms seen in depression and dementia, with a brief discussion about their more typical presentation in each disorder.

Conclusion and Treatment Issues

Sometimes it is very difficult to make a firm diagnosis of depression in the context of dementia, especially when the dementia is very advanced. The clinician will occasionally choose to instigate treatment regardless of diagnostic certainty, weighing the possible benefits versus potential adverse outcomes of treatment.

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