



Assessing and managing depression in patients with dementia

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Abstract

The relationship between depression and dementia is complex. Depression appears to be an independent risk factor for incident dementia, conferring a two-fold increase in dementia risk. Depression may represent an early sign or prodromal feature of dementia. The association between depression and dementia appears to strengthen as the interval between the two disorders shortens. Depression may also be a consequence of dementia. It is difficult to determine whether this represents a biological sequela of neurodegeneration, or a psychological response to cognitive and functional impairment or associated social factors such as a move to residential care. Assessment of depression in older people with dementia can be challenging. Individuals with dysphasia may struggle to express their thoughts and feelings, in which case there should be a greater focus on changes in behaviour, such as tearfulness, irritability, seclusion, or disengagement from hobbies and activities. Somatic symptoms such as fatigue, sleep disturbance, and GI discomfort are more common in older people with depression than in their younger counterparts; and although investigations for other causes should be pursued, the possibility of depression should be borne in mind. When making a diagnosis of depression in older patients it is important to screen for an underlying physical condition, in particular endocrine disorders, occult malignancy and nutritional deficiencies.

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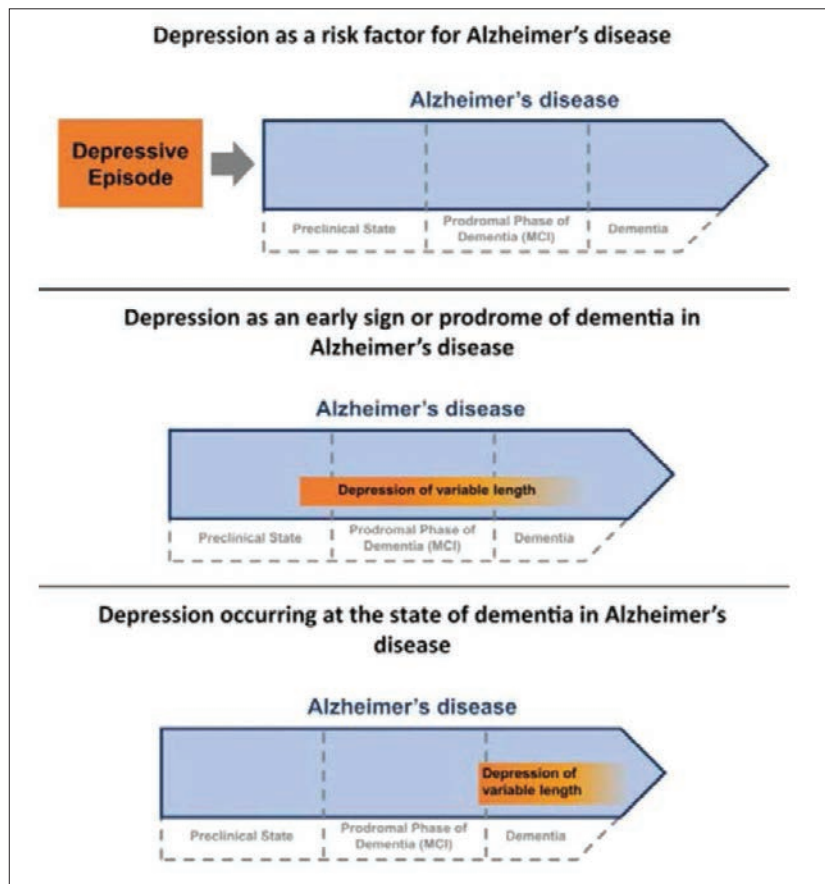
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FIGURE 1

The temporal relationship between depression and dementia. Reproduced from Dafsari FS, Jessen F. Depression – an underrecognized target for prevention of dementia in Alzheimer's disease. *Transl Psychiatry* 2020;10(1):1-3⁶ (CC 4.0 License)



DEPRESSIVE SYMPTOMS ARE COMMON IN LATER LIFE.¹ DEPRESSION IS ASSOCIATED WITH HIGHER RELAPSE

rates, and a more protracted course, than depression in individuals in midlife.^{1,2}

There are currently 900,000 people in the UK, and 50 million people worldwide, living with dementia.^{3,4} Although characterised by a progressive decline in functional and cognitive ability, it is the neuropsychiatric symptoms associated with dementia, such as depression, that correlate most closely with rates of carer stress.⁵

DEMENTIA AND DEPRESSION

An association between depression and dementia has long been observed, but the relationship between the disorders is complex (see figure 1, above).⁶

Depression appears to be an independent risk factor for incident dementia, conferring a two-fold increase

in dementia risk.⁷ This risk is not confined to depression in older age.

Individuals with depression in both the Framingham Heart Study (mean age at baseline 71.5 ± 8 years) and the Baltimore Longitudinal Cohort of Aging (mean age at baseline 55.5 ± 18.8 years) were more likely to have been diagnosed with dementia over follow-up periods lasting 17 and 24 years, respectively.⁸

As a potentially modifiable risk factor, depression has been cited as an important focus for dementia prevention.⁹

Depression can represent an early sign or prodromal feature of dementia. Since neuropathological substrates of many dementia subtypes, such as Alzheimer's disease (AD), can be detected in the brains of affected patients ten years or more before clinical presentation, non-cognitive presentations, such as depressive illness have been hypothesised as a harbinger of eventual

Is depression a risk factor for dementia?

How should patients be assessed?

What are the management approaches?

dementia. The association between depression and dementia appears to strengthen as the duration between the two disorders shortens.¹⁰ Depressive symptoms in cognitively healthy individuals recruited to the Italian Longitudinal Study on Aging were predictive of global cognitive decline and episodic memory disturbances within four years.¹¹

Depression may also be a consequence of dementia. It is difficult to determine whether this represents a biological sequela of neurodegeneration, or a psychological response to cognitive and functional impairment or associated social factors such as a move to residential care. Rates of depression in people with mild, moderate and severe dementia often exceed those in cognitively healthy older people.¹²

In the case of dementia with Lewy bodies, the second most common form of neurodegenerative dementia,^{13,14}



depression is integrated into the clinical diagnostic criteria for the disease.¹⁴

There is also a possibility that dementia and depression, as two prevalent and multifactorial disorders, may independently coexist through common combinations of biological, psychological, cultural, and social risk factors. Many of these risk factors, such as social isolation, medical comorbidities and sensory impairment, are themselves associated with age. This appears less likely as new epidemiological evidence regarding the relationship between depression and dementia, such as that described above, emerges.

The proposed biological mechanisms underpinning depression are complex and poorly understood, and discussion of these is beyond the scope of this article. Some proposed models of depression do share characteristics commonly implicated in neurodegenerative disease, such as vascular injury,¹⁵ inflammation,¹⁶ and elevated glucocorticoid production.¹⁷

As dementia represents a heterogeneous group of disorders, each with different pathophysiological mechanisms, it is unlikely that any single process, or group of processes, is responsible for depressive illness in the context of neurodegenerative disease.

Uncertainty over the nature of the relationship between depression and dementia has led to a reduction in the use of the term pseudodementia.¹⁸ Psychiatric disorders, depression included, are often associated with cognitive symptoms in older people,

and can therefore be mistaken for the symptoms of neurodegenerative disease. It nevertheless remains a valid construct; a systematic review of 18 studies, comprising 284 participants, found that 53% of patients with pseudodementia did not meet criteria for dementia at follow-up.¹⁸

This potential for reversibility of cognitive symptoms supports the practice of assessing all patients with suspected dementia for depressive illness prior to any diagnosis.¹⁹

DIAGNOSING DEPRESSION IN THE CONTEXT OF DEMENTIA

The diagnostic criteria for depression do not vary with age or dementia diagnosis. In order to fulfil core ICD-10 criteria for depression, patients must have any two of the following symptoms: depressed mood, loss of interest and enjoyment, and reduced energy for at least a period of 2 weeks (see table 1, below).⁴ Episodes are usually classified according to their severity (mild, moderate, or severe) on the basis of the number of symptoms as well as the degree of functional impairment.⁴

Assessment of depression in older people with dementia can be challenging, particularly as presentation may be less typical than in younger adults. Individuals with dysphasia may struggle to express their thoughts and feelings during assessment. In such cases, there should be a greater focus on changes in behaviour, such as tearfulness, irritability, seclusion, or disengagement from hobbies and activities.¹⁹ Collateral history is crucial.

Somatic depressive symptoms (such as gastrointestinal discomfort, fatigue and sleep disturbance) are more commonly seen in older people with depression than in their younger counterparts,²⁰ and although investigations into other causes of such symptoms should be pursued, the possibility that they represent depressive illness should continue to be borne in mind. When making a diagnosis of depression in older patients it is important to screen for an underlying physical condition, in particular endocrine disorders, occult malignancy and nutritional deficiencies.

Assessment is further complicated by the prevalence of apathy in neurodegenerative disorders. Defined as the absence of feeling, motivation, emotion, interest or concern,²¹ apathy in dementia is often confused with depression in the context of dementia and it can be difficult to differentiate between them because of the overlap in core symptoms.²²

Apathy can coexist with depression, but can also appear independently, manifested as lack of motivation or interest, a lack of concern about personal problems, or an absence of emotional response to positive or negative personal events. Apathy tends to respond less favourably than depression to pharmacological therapy.²²

Depression rating scales in dementia

Validated rating scales can be useful as part of a systematic approach to the assessment of depression in people with dementia. Such scales do not, however, replace clinical assessment; they do not assess risk, or account for marked sensory or language impairment.

The two most frequently used scales in research studies are the 15-point Geriatric Depression Scale (GDS-15)²³ and the Cornell Scale for Depression in Dementia (CSDD). The GDS-15 is a self-rated scale initially designed for depression screening in populations without dementia. The CSDD was designed for patients with dementia, requiring two semi-structured interviews with the informant and the patient.

The main disadvantage in the primary care setting is the time required to administer these instruments; although the 4-point and 5-point versions of GDS (GDS-4, GDS-5) are much briefer, estimates of their sensitivity and specificity are heterogeneous, and the evidence generally low in quality.²⁴ The authors would therefore recommend that while rating scales provide helpful frameworks for assessment, they should not be used routinely in primary care.

Table 1

Summary of the ICD-10 criteria for depression⁴

Symptoms must be present for at least two weeks

At least 2 of the following core symptoms must be present (all 3 in severe episodes):

- Depressed mood
- Reduced energy/increased fatiguability
- Anhedonia/loss of pleasure and interest

In addition, other symptoms must be present (2 present in mild, 3-4 in moderate and > 4 in severe episodes):

- Reduced concentration and attention
- Reduced self-esteem and self-confidence
- Ideas of guilt and worthlessness
- Bleak and pessimistic view of the future
- Ideas or acts of self-harm or suicide
- Disturbed sleep
- Diminished appetite

Severe depressive episode with psychotic symptoms: As well as meeting the criteria above for a severe depressive episode, there will also be delusions, hallucinations or depressive stupor present

key points

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Depressive symptoms are common in later life.

Late life depression is associated with higher relapse rates and a more protracted course than mid-life depression. The relationship between depression and dementia is complex. Depression appears to be an independent risk factor for incident dementia, conferring a two-fold increase in dementia risk. Depression may represent an early sign or prodromal feature of dementia. The association between depression and dementia appears to strengthen as the interval between the two disorders shortens.

Depression may also be a consequence of dementia.

It is difficult to determine whether this represents a biological sequela of neurodegeneration, or a psychological response to cognitive and functional impairment or associated social factors such as a move to residential care.

Despite a reduction in its use, the term pseudodementia

remains a valid construct; a systematic review found that 53% of patients with pseudodementia did not meet criteria for dementia at follow-up. This potential for reversibility of cognitive symptoms supports the practice of assessing all patients with suspected dementia for depressive illness prior to diagnosis.

The diagnostic criteria for depression do not vary with

age or dementia diagnosis. However, assessment of depression in older people with dementia can be challenging. Individuals with dysphasia may struggle to express their thoughts and feelings, in which case there should be a greater focus on changes in behaviour, such as tearfulness, irritability, seclusion, or disengagement from hobbies and activities. Somatic symptoms such as gastrointestinal discomfort, fatigue and sleep disturbance, are more commonly seen in older people with depression than in their younger counterparts; and although investigations into other causes of such symptoms should be pursued, the possibility that they represent depressive illness should continue to be borne in mind. When making a diagnosis of depression in older patients it is important to screen for an underlying physical condition, in particular endocrine disorders, occult malignancy and nutritional deficiencies.

A recent Cochrane review of antidepressants for

depression in dementia concluded that little or no effect was observed on the only measure of efficacy for which high-quality evidence was available (depression rating scale scores). A review of psychological therapies found a small reduction in depressive symptoms and increased rates of remission with CBT-based treatments. In rare cases where it is felt that the benefits of pharmacological therapy may outweigh the risks, referral to the old age psychiatry service should be considered. Cognitive stimulation therapy is associated with improved quality of life in participants with dementia, and music-based therapies have demonstrated benefits in depression scores and quality of life.

MANAGING DEPRESSION IN PATIENTS WITH DEMENTIA

Pharmacological treatments

There are several important considerations when prescribing pharmacological treatments in patients with dementia.

Clinical trials of antidepressants have historically failed to include older adults, use rating scales designed for younger adults and caution should be employed when generalising data to older populations.

Recent systematic reviews of antidepressants for depressive disorder in older adults have included 15 or fewer randomised controlled trials (RCTs).^{25,26} Several of these RCTs have investigated tricyclic antidepressants (e.g. amitriptyline, clomipramine), which can exacerbate cognitive impairment through their anticholinergic effects,¹⁹ and therefore should be avoided if possible in individuals with dementia. Other RCTs have been adjudged to be of low or moderate quality.²⁵

The response rates to antidepressants in these RCTs vary considerably,²⁶ and some meta-analyses report no benefit of antidepressant therapy over placebo in older adults,²⁷ and that the risk of adverse events outweighed the benefits.

A recent Cochrane review of antidepressants for depression in dementia concluded that little or no effect was observed on the only measure of efficacy for which high quality evidence was available (depression rating scale scores).²⁸

NICE guidelines advise that antidepressant therapy should not be offered to manage mild to moderate depression in people with dementia, 'unless indicated for a pre-existing severe mental health problem'.¹⁹

GPs will be aware of the many pitfalls encountered in prescribing for older people including polypharmacy, adverse events, drug interactions and falls; all of these are encountered with antidepressants.²⁹

In rare cases where the benefits of pharmacological therapy are felt to outweigh the risks, choice of individual agents should involve discussion with the patient and caregiver regarding the side effect profile and treatment targets. Referral to the local psychiatry of old age service should be considered. Doses should 'start low and go slow' and there should be a low threshold for cessation if side effects emerge or no benefit is seen.

Non-pharmacological interventions

Given the limitations of pharmacological therapy, NICE guidelines for dementia

advocate consideration of psychological therapies for the treatment of mild to moderate depression.¹⁹

A recent Cochrane review of 24 studies assessing the clinical effectiveness of psychological therapies for depression and anxiety in dementia found that cognitive behaviour therapies reduce depressive symptoms more than treatment as usual and increase rates of remission, albeit with small effect sizes noted.³⁰

They may also improve quality of life and activities of daily living when compared with treatment as usual or active control (such as non-structured non-pharmacological contact e.g. attention from staff or social contact).

There were insufficient data on interpersonal therapy and mindfulness-based cognitive therapy from which to draw conclusions.

Other non-pharmacological interventions have shown promise in the management of depression in dementia, particularly those more accessible to patients with cognitive impairment, and arguably easier to deliver at a service or community level.

Cognitive stimulation therapy, defined as activities and discussions aimed at general enhancement of cognitive and social functioning, is associated with improved quality of life in participants with dementia.³¹ Cognitive stimulation therapy is offered on a group basis by 96% of UK memory clinic services, and on an individual basis in 53% of services.³²

Music-based therapies have demonstrated benefits in depression scores and quality of life,³¹ while other non-pharmacological interventions, such as light therapy, occupational therapy, massage therapy or exercise programmes, while not supported by comparable bodies of evidence for efficacy, are well tolerated.

Referral to day centres for people with dementia may be a useful way for patients to access non-pharmacological interventions.

These 'social prescribing' opportunities can help facilitate social engagement and can build peer support networks as well as potentially alleviate symptoms.³³

CONCLUSION

Although the relationship between the two conditions is poorly understood, depression is common in patients with dementia and significantly impacts on the quality of life of those affected. The risk:benefit ratio does not generally favour pharmacological therapy, but social prescription and structured psychological therapies, which appear >>

to be associated with less risk, are recommended.

Competing interests: None

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Useful information

For patients

Royal College of Psychiatrists
www.rcpsych.ac.uk/mental-health/problems-disorders/depression-in-older-adults

Alzheimer's Society

www.alzheimers.org.uk/about-dementia/symptoms-and-diagnosis/depression-dementia

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