

Medical News & Perspectives

Exploring the Relationship Between Depression and Dementia

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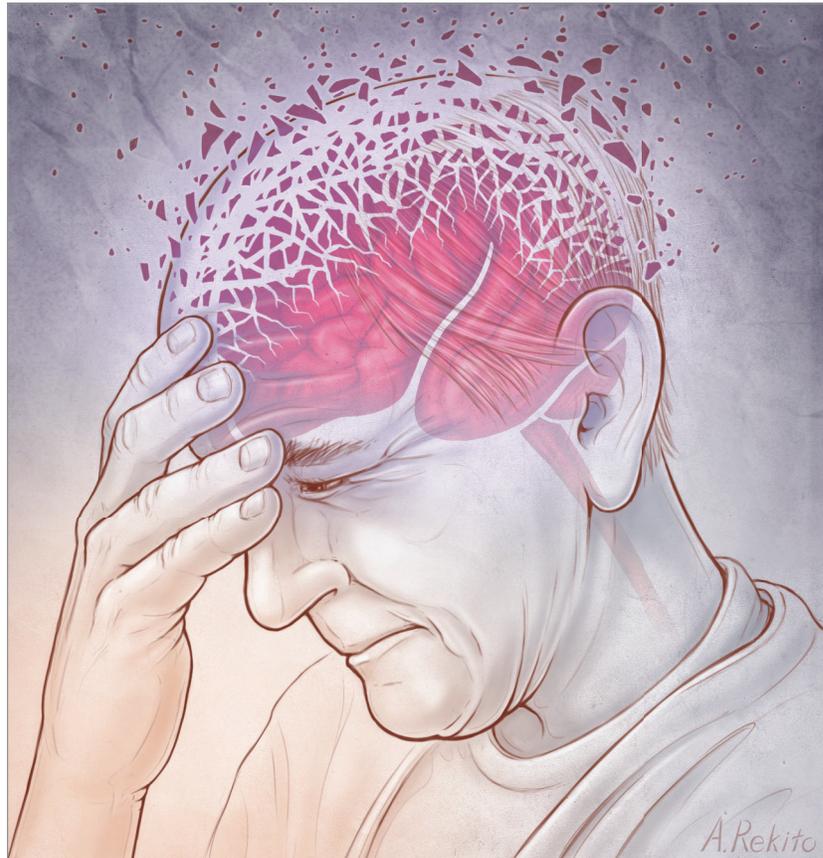
Diagnosing and treating depression in people with mild cognitive impairment (MCI) or with dementia presents special challenges, but doing so can improve the quality of their lives as well as the lives of their caregivers and, in the case of MCI, might even delay progression to dementia.

Researchers are still trying to tease out the relationship between depression and dementia. While depression does not appear to cause dementia, it likely is a risk factor, just as dementia is a risk factor for depression, said George Alexopoulos, MD, founder and director of the Weill-Cornell Institute of Geriatric Psychiatry. At least 20% of people with dementia develop a depressive syndrome, Alexopoulos said.

Often, though, the depression comes first. Some studies suggest that depression in early life is a risk factor for dementia, while depression later in life can be a prodrome of dementia, Alexopoulos said. Although findings are mixed, a 2014 [review](#) of the literature concluded that there is convincing evidence to suggest that depression can be a risk factor and a prodromal symptom of dementia.

In a more recent large longitudinal cohort [study](#) published in 2017 in *JAMA Psychiatry*, researchers followed the trajectory of depressive symptoms and dementia in 10 189 UK men and women over 28 years. Unlike some previous studies, this one found that depressive symptoms in midlife, even if chronic or recurring, were not associated with an increased risk of dementia. However, participants with depressive symptoms later in life had a higher risk of dementia. Depressive symptoms appear to be a prodromal feature of dementia or, perhaps, share common causes, such as neurodegeneration and inflammation, but they do not appear to increase the risk of dementia, according to the authors.

In contrast, another longitudinal [study](#) involving 4992 older Australian men, published 2 months earlier, found that those



who had a history of depression earlier in life did have a higher risk of dementia than those who did not. However, the association was greater in men who were depressed when they entered the study. Treatment with antidepressants did not decrease the risk of depression-associated dementia, leading the authors to conclude that late-life depression should be considered an early sign of dementia, not a modifiable risk factor.

"Any time you have the first episode (of depression) at a later age, that's always concerning for a neurodegenerative disorder," said Anna Burke, MD, a geriatric psychiatrist and the director of neuropsychiatry at Barrow Neurological Institute in Phoenix, who was not involved with either study.

Raj Shah, MD, an associate professor of family medicine with the Rush University

Alzheimer Disease Center in Chicago, recommends that a first episode of depression in older individuals be considered a sentinel event, the same way a fall is. Both events should spur questions about whether patients need to have their medication adjusted or whether the fall or the mood change is a marker of other conditions, Shah said.

Difficult Diagnosis

Depression is often overlooked when it accompanies dementia, Burke said.

"The problem is the *DSM-5* [*Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition)] criteria we use for major depressive disorder don't necessarily fit for this population, much like in children, where depression presents differently," she said.

As with children, adults living with dementia and depression might not talk about emotional pain or feeling down, Burke said. Instead, they might exhibit irritability—"they may just get a little more feisty," she said—and an increase in somatic symptoms, such as aches and pains and gastrointestinal complaints.

"Sometimes people don't get diagnosed with depression because there is such a huge overlap in symptoms between depression and dementia as well as growing older," Burke said. Symptoms common to both depression and dementia include loss of interest in activities and hobbies, social withdrawal, and impaired thinking.

Because the symptoms overlap, caregivers might not recognize depression in people with dementia. "I'm often the first person to bring it up," Burke said. "Even when people do seek treatment in the community, many physicians are not focused on treating anything beyond the memory changes. Nobody ever really discusses the behavioral changes, the changes in mood."

Still, Alexopoulos said, "If you see the patient at the wrong time, you may miss it. Patients with dementia underreport depression, and caregivers are unreliable reporters."

As David Steffens, MD, MHS, explained, "It's hard to notice a change in mood when somebody can't really voice how they're feeling."

But that doesn't mean depression is insignificant in the setting of dementia. "One reason to treat depression is that depression makes underlying cognitive impairment much worse," said Steffens, chairman of psychiatry at the University of Connecticut. "You want to give them their best cognitive chance." Besides antidepressants, he said, psychiatrists have sometimes used electroconvulsive therapy to treat severe depression in people with mild dementia.

Drug Therapy

The prescribing of antidepressants to people with dementia appears to be increasing, according to a UK [study](#) published in 2017. Trends in diagnosis and treatment of people with dementia suggest that the proportion prescribed antidepressants rose from 28% to 36.6% from 2005 to 2015.

Antidepressants don't seem to work as well in people with dementia, possibly because "depression in dementia is a different illness" than depression in people with normal cognition, Alexopoulos said. Cognitive control dysfunction in dementia appears to decrease the effectiveness of some selective serotonin reuptake inhibitors (SSRIs), he and his coauthors wrote in a 2015 [article](#). "I think it is appropriate to try to treat with as little medication as you can," in part because polypharmacy can lead to delirium syndromes in patients with dementia, Alexopoulos said.

Although the study of Australian men found that taking antidepressants did not reduce the risk of depression-associated dementia, recent research suggests that the drugs might slow the progression to dementia in people with MCI and depression. That [study](#), published in 2017, found that taking the antidepressant citalopram (Celexa), an SSRI, for more than 4 years was associated with a delay in progression from MCI to Alzheimer disease by about 3 years. "Three years is a big deal in this age group," Alexopoulos said. [Experiments](#) in mice and healthy humans have shown that citalopram reduces amyloid plaque, one of the hallmarks of Alzheimer disease.

Treating depression in people with MCI with antidepressants might slow the progression to dementia, but little is known about whether drugs and other interventions developed to treat Alzheimer disease have any effect on depression.

Most clinical trials of potential Alzheimer disease treatments do not consider neuropsychiatric symptoms such as depression or irritability as primary research targets, even though "these symptoms are widely recognized as the most stressful and challenging manifestations of dementia," concluded authors of a recent [review article](#). Only 17.7% of the relevant studies they found on [clinicaltrials.gov](#) tested the effect of pharmacological or nonpharmacological interventions on neuropsychiatric symptoms, they wrote.

Beyond Medication and Talk Therapy

People with MCI might still be able to benefit from cognitive behavioral therapy or psychotherapy, but that becomes less likely

as they decline, Burke said. "A huge part of psychotherapy is being able to remember what happened in a session."

Even individuals whose dementia is too advanced for talk therapy can still benefit from lifestyle changes, though, Burke said. Engaging them in social activities and modifying their environment to minimize triggers that make them anxious or irritable can help improve their quality of life, she said.

A recent pilot [study](#) suggested that increasing exposure to daylight can reduce depression in people with dementia. The 12-week study involved 77 people living in 8 dementia care communities. At 4 of the communities, staff took study participants to a room with windows for socialization from 8 AM to 10 AM each day. At the other 4 communities, staff took study participants to socialize in the mornings in a room illuminated only with typical artificial light.

At the end of the study, participants who had socialized in the rooms with daylight had a statistically significant decrease in their scores on the [Cornell Scale for Depression in Dementia](#), while the other participants did not. More studies are needed to determine the appropriate timing, duration, wavelength, and intensity of light exposure for adults with dementia, the researchers concluded.

Another recent [study](#) suggested a perceived lack of social engagement is also associated with depressive symptoms in people with dementia. Researchers measured social engagement, medication use, and depressive symptoms in 402 community-dwelling adults whose average age was 86 years. The data were collected during the first interview at which the participants met the criteria for a dementia diagnosis. The researchers found a link between perceived social isolation and the severity of depressive symptoms but not between antidepressant use and severity of depressive symptoms.

Because the study participants were newly diagnosed, their dementia was mild to moderate. "At that stage, people can still engage," coauthor Shah said. "If we break down some of the stigma around the diagnosis of dementia, it will help people build cultures of support and inclusiveness." ■

Note: Source references are available through embedded hyperlinks in the article text online.