What’s causing my older patient’s cognitive decline?

Changes related to aging alone typically don’t interfere with one’s ability to function independently. These tips and tools can help ensure an accurate evaluation.

CASE

A 68-year-old woman with a history of well-controlled hypertension and diabetes presents to the office for routine follow-up. She says she has adhered to her current medications, and her blood pressure and hemoglobin A1c remain at goal. At the close of the visit, she mentions that she is worried she may be developing dementia. She says she has been having difficulty finding the right word in conversation and needs to write things down more than she used to.

What might be causing this patient’s changes in cognition?

In primary care settings, when patients complain of memory loss, there is a 20% to 30% chance they will be found to have mild cognitive impairment (MCI) or some level of dementia.1 Given the significant consequences of dementia, it’s important to maximize opportunities to distinguish those with age-related changes in cognition or reversible causes of memory loss from those who have irreversible pathologic changes.

Age-related changes in cognition

Changes in cognition associated with aging vary considerably among individuals and across domains of cognition. By their 7th decade, most people experience a decline in processing speed and working memory.2 However, some individuals retain excellent function into their 80s and perform as well as younger adults.3

Changes long thought to be due to brain senescence may, in fact, be related to the effects of age-related medical conditions on the brain’s function.4 Consistent with this theory is the observation that cognitive changes tend to occur earlier in individuals with cardiovascular disease, diabetes, and cancer.2 What constitutes a normal change depends on an individual’s baseline cognitive function, educational background, medical comorbidities, and the potential impact of sensory impairment on performance.
General cognitive trends with aging. Awareness of normal changes in an aging population is useful when assessing patients concerned about their memory. In general, an individual’s ability to maintain attention to a single task is preserved into late life. Ability to perform tasks requiring divided attention or attention-switching tends to decline. This has implications for driving, given the need to constantly switch one’s attention in response to the environment and the ability to sort relevant from irrelevant information.

Remote memory, semantic memory (factual information), and procedural memory (knowledge of skills and procedures) tend to remain intact with aging. Short-term memory (simple maintenance of information over a short period of time) shows little change with aging. However, working memory, which requires the manipulation of information in short-term memory, declines.

A simple demonstration of this is that performance on digit span testing tends to remain preserved (7±2), but digit span backwards declines. Holding digits in mind in the order they are received can be achieved through rehearsal. But to reverse the order requires reorganization of the information, and this ability declines with aging. Prospective memory (remembering to do things in the future) often requires increased dependence on external aids, such as a to-do list. The capacity to learn and recall new information declines. Even when given repeated opportunity to practice, older adults demonstrate a slower learning curve and lower total amount learned. Therefore, it becomes easier relying on well-learned cognitive processes such as cooking a familiar meal or relying on previously used principles for decision making.

Language comprehension and vocabulary remain stable over time. However, difficulty with spontaneous word finding—the “tip-of-the-tongue” phenomenon—tends to increase. In contrast to the dysnomia related...
Cognitive changes with aging typically do not interfere with an individual's ability to function independently.

Mild cognitive impairment/-mild neurocognitive disorder

Originally conceived as a precursor to Alzheimer's dementia, mild cognitive impairment (MCI) is a diagnosis that has evolved to describe a heterogeneous syndrome of abnormal cognition characterized by:

- a suspected change in cognition expressed by the patient, an acquaintance who knows the patient well, or a clinician;
- objectively measured impairment in one or more cognitive domains beyond what would be expected based on an individual's age and educational background;
- preservation of functional abilities; and
- a lack of findings that would fulfill criteria for dementia.

In the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM V), this concept is identified as mild neurocognitive disorder, with the additional caveats that an individual's cognitive deficits do not occur exclusively in the context of delirium and are not better explained by another mental disorder such as depression or schizophrenia.

An accurate assessment of cognitive change is best measured against the individual's baseline, which may necessitate the report of a reliable acquaintance. An assessment of functional abilities is also critical. Mild problems in performing complex functions (bill paying, shopping, etc) could be present and still allow a patient to meet the criteria for MCI. An individual may take more time, be less efficient, or make more errors than before; however, independence with minimal aid or assistance is preserved. It can be difficult to distinguish MCI from the effects of normal aging particularly on a single assessment, and serial evaluations can be beneficial.

MCI can be divided into 4 subtypes depending upon the cognitive domains affected (complex attention, executive function, learning and memory, language, visuospatial, social cognition):

1. Amnestic MCI single domain, if only memory is affected.
2. Amnestic MCI multiple domain, if memory and any other cognitive domains are affected.
3. Non-amnestic MCI single domain, if any other cognitive domain aside from memory is the only one affected.
4. Non-amnestic MCI multiple domain, if multiple domains other than memory are affected.

These distinctions may provide clues to the underlying cause of dysfunction and provide prognostic information regarding the risk of progression to dementia.

Prevalence estimates for MCI vary widely due to differences in definitions used and populations studied. The best estimate is 5% to 10% prevalence among those ages 65 to 69 years old, and 12% to 25% among those ages 80 to 84. Similarly, estimates of the rate of progression to dementia vary. Among MCI populations identified through referral sources such as memory centers, the rate of progression to dementia has been 10% to 15% per year. In epidemiologic studies of general populations, the rate has been 6% to 10% per year. The rate of development of dementia among normal subjects is 1% to 2% per year.

Dementia/major neurocognitive disorder

The primary feature distinguishing MCI/mild
neurocognitive disorder from dementia or major neurocognitive disorder is a patient’s functional status. The core clinical criteria for all-cause dementia are cognitive or neurobehavioral symptoms that:

- interfere with work or usual daily function,
- represent a change from the prior baseline function,
- are not explained by delirium or a psychiatric illness, and
- include detectable impairment in 2 cognitive domains.

Criteria outlined in the DSM-V for major neurocognitive disorder are essentially the same but describe the functional change criteria as cognitive changes that “interfere with independence in everyday activities.” The DSM-V elaborates: “at a minimum, requiring assistance with complex instrumental activities of daily living such as paying bills or managing medications.”

Assessing functional status accurately in clinical practice typically requires the assistance of a collateral informant who knows the patient well. The Informant Questionnaire on Cognitive Decline in the Elderly (https://www.alz.org/documents_custom/shortcode_english.pdf) is one validated assessment tool that can be used for this purpose. With this self-administered form, the informant answers 16 questions regarding changes in the patient’s performance of different activities over the 10 years prior. Alternatively, a structured interview based on indices of activities of daily living (ADLs) and instrumental activities of daily living (IADLs) as listed in TABLE 1 can be employed.

Review of the various causes of dementia is beyond the scope of this article, but a list of common diagnoses is presented in TABLE 2.

**TABLE 1**

Impairment of these activities suggests cognitive decline

<table>
<thead>
<tr>
<th>Activities of daily living</th>
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<tbody>
<tr>
<td>Bathing, dressing, toileting/continence,</td>
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<tr>
<td>transferring/ambulation, and eating</td>
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</tbody>
</table>

<table>
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<tr>
<th>Instrumental activities of daily living</th>
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<tbody>
<tr>
<td>Ability to use the telephone, shopping, food</td>
</tr>
<tr>
<td>preparation, housekeeping, laundry, mode of</td>
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<tr>
<td>transportation, responsibility for own</td>
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<tr>
<td>medication, and ability to handle finances</td>
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**TABLE 2**

Possible causes of dementia

<table>
<thead>
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<th>Possible causes of dementia</th>
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<tbody>
<tr>
<td>Alzheimer’s disease</td>
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<tr>
<td>Creutzfeldt-Jakob disease</td>
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<tr>
<td>Dementia with Lewy bodies</td>
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<tr>
<td>Frontotemporal dementia (also known as</td>
</tr>
<tr>
<td>frontotemporal lobar degeneration)</td>
</tr>
<tr>
<td>HIV-related encephalopathy</td>
</tr>
<tr>
<td>Mixed dementia</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
</tr>
<tr>
<td>Traumatic brain injury</td>
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<tr>
<td>Vascular dementia</td>
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<tr>
<td>Wernicke-Korsakoff syndrome</td>
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HIV, human immunodeficiency virus.

Elderly patients with depression commonly complain of memory impairment, and this interaction between depression and dementia has been investigated for decades. The term “pseudodementia” has been used since 1961 to describe signs of dementia in a patient with any psychiatric illness, but it has since been refined to apply solely to depression. The prevalence of depression among older adults varies depending on the population studied and how depression is defined. Approximately 2% to 3% of community-dwelling elders meet criteria for major depression, with 10% to 30% showing some symptoms of depression.

Twenty percent to 40% of elderly patients diagnosed with depression will have evidence of cognitive impairment.

A broad range of cognitive deficits have been associated with depression. Most consistently described are deficits in processing speed, attention, and executive function. Memory deficits can be apparent...
Distinguishing mild cognitive impairment from normal effects of aging may require serial evaluations following an initial assessment.

with tests of delayed recall, but recognition (the ability to identify items from a list) generally is preserved. Distinguishing between pseudodementia and true dementia can be challenging. An increased severity of deficits, particularly with delayed recall, is more indicative of dementia. Additionally, on clock drawing tasks, individuals with depression perform more comparably to controls than do those with true dementia.

A 2013 meta-analysis reported a significant association of late-life depression with subsequent development of dementia, with an odds ratio (OR) of 1.85. The risk of subsequently developing vascular dementia (OR=2.52) was significantly higher than that for Alzheimer’s disease (OR=1.65). Individuals with evidence of reversible cognitive impairment at the time of diagnosis of depression seem to be particularly vulnerable, with dementia developing in 43% to 71%, compared with rates of 12% to 18% among elders diagnosed with depression but lacking signs of cognitive impairment.

Other causes of reversible dementia
A meta-analysis performed in 1988 found that 11% of cases of dementia were reversible. However, an update using the same methodology in 2003 revealed the number had dropped to less than 1%. In the latest meta-analysis, one of the authors’ leading hypotheses for the dramatic decline in apparent prevalence was a significant shift in the study population from the inpatient to outpatient setting. In studies of community-based populations used in the re-analysis, the reported prevalence of reversibility was near zero.

Metabolic abnormalities—most often B₁₂ deficiency and hypothyroidism—are commonly cited as potential causes of dementia. Four systematic reviews, including one conducted by the Cochrane Collaborative, concluded there is a lack of evidence that treating low vitamin B₁₂ in individuals with dementia improves cognition. There is some evidence, though, of a time-limited window for successful treatment within 12 months of the onset of symptoms. A study reviewing causes of dementia in nearly 3000 individuals found one case of reversible dementia attributable to hypothyroidism. A subsequent review reached similar conclusions about the lack of data to support the notion that treatment of hypothyroidism reverses dementia.

Similarly, imaging for cerebral tumors, subdural hematomas, or normal-pressure hydrocephalus rarely identifies these as a cause of dementia. This is particularly true of unselected community-based populations, as there are typically signs or symptoms suggesting an intracranial pathology.

Numerous medications have been implicated in causing acute confusional states, and there is some evidence for their role in chronic confusion (TABLE 3). In my experience, many who experience adverse effects on cognition with medications will also have an underlying neurodegenerative process, and symptoms do not completely resolve with withdrawal of the offending agent.

CASE
Further assessment of the patient yielded a score of 29/30 on the Montreal Cognitive Assessment* and a zero on the Patient Health Questionnaire-2. Careful review of her daily function revealed no significant deficits in ADL or IADL performance, and her daughter confirmed that she had not observed any significant decline in her mother’s function. There was no significant family history of dementia. The patient was reassured that her cognitive changes were normal and age related.

Unfortunately, few data support specific interventions to reduce this patient’s risk of developing dementia. She was commended for keeping her blood pressure and blood sugar levels under control, thereby reducing her risk of vascular disease.

She and her daughter were directed to the Alzheimer’s Association Web site (alz.org) as a resource for information about signs and symptoms to watch for and for caregiv-

*The Montreal Cognitive Assessment is a validated office-based tool for the evaluation of cognitive impairment that is highly sensitive for the detection of mild cognitive impairment.
TABLE 3
Medications associated with cognitive impairment*42,43

| Anticholinergics (diphenhydramine, hydroxyzine, meclizine, promethazine) |
| Antidepressants (TCAs, particularly those with anticholinergic effects such as amitriptyline; SSRIs, which are generally low risk, although paroxetine should be avoided) |
| Benzodiazepines (class effect, worse with long-acting agents such as diazepam) |
| H2-receptor antagonists |
| Nonbenzodiazepine, benzodiazepine receptor agonist hypnotics (eg, zolpidem) |

SSRIs, selective serotonin reuptake inhibitors; TCAs, tricyclic antidepressants.

*This list is not exhaustive.

ing resources, should they be needed. She was briefly counseled to eliminate distractions to improve her ability to complete tasks and improve recall along with rehearsing or writing down information that she wished to retain.

Finally, she was counseled to remain physically, cognitively, and socially active as these are factors generally associated with healthy aging, have some evidence to support efficacy in reducing the risk of cognitive decline, and are unlikely to be of harm.

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References

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For more on healthy aging, listen to: “How much can we really do to slow cognitive decline,” at: http://bit.ly/2ghoQKw.
Treating an Alzheimer’s patient? 6 tips from a patient’s spouse

The author’s wife struggled with Alzheimer’s disease for 10 years. The insights he provides here are drawn from his experience—and the literature.

What’s it like to be the caregiver for an Alzheimer’s patient? In my case, it was like being both married and widowed at the same time. Or as a person in my support group once put it: It’s a life filled with grief on the installment plan.

My wife, Clare, struggled for nearly 10 years with Alzheimer’s disease before passing away in April 2016—just one month shy of her 70th birthday and 2 months shy of our 49th wedding anniversary.

Our experience was gut-wrenching, but not unique for families coping with Alzheimer’s disease. Life as a caregiver is one of non-stop daily stress, with much sadness and anxiety, often accompanied by periods of mild or serious depression. Doubt, guilt, frustration, and many other emotions lead many caregivers to take anti-anxiety or antidepressant medication, meet regularly with therapists, take sleeping pills, or experience significant weight gain or loss. Stress drove me to my comfort foods, and I gained nearly 100 pounds while caring for Clare. Only in the last few months have I been able to start taking off that weight.

Helping a loved one who has Alzheimer’s with even the basic activities of daily living—hygiene, dressing, eating—becomes progressively difficult. Caring for a loved one who is confused, no longer remembers your name or who you are, or can occasionally become aggressive, is emotionally painful.

After being Clare’s 24/7 caregiver for 6 years, I agreed that placement in an assisted living facility was in her best interest. My role morphed from primary caregiver to primary care advocate, but the stress did not lessen. I met regularly with facility staff to ensure proper care because many staff members were not sufficiently motivated, educated, or trained to consistently provide proper care for individuals with Alzheimer’s disease.

Financial stress weighs heavily on caregivers. Unless one qualifies for Medicaid, is very wealthy, or is lucky enough to have outstanding long-term health care insurance and prescription drug coverage, caregiving...