Chapter 35
Memory Loss/Cognitive Impairment

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Introduction

Memory loss and cognitive impairment become more common with increasing age and as the number of persons aged 65 years and older continues to rise (projected to be 25% of US population by 2040), so too does the need for evaluation and management of cognitive issues in the ambulatory setting. Early diagnosis and timely intervention for probable dementia has several benefits including early initiation of treatment, institution of safety measures, and provision of caregiver support and training. This section will outline the evidence-based evaluation, differential diagnosis, and management of memory loss and cognitive impairment.

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Key History and Physical Exam/Decision-Making

While the United States Preventive Services Task Force (USPSTF) does not currently recommend routine screening of asymptomatic patients for cognitive impairment (2014 USPSTF Panel recommendation) [1], many consider it best practice for providers to ask their older patients if they are experiencing memory and cognitive difficulties. Additionally, since some patients with cognitive impairment may lack awareness or insight into their loss, primary care providers need to be vigilant for the appearance of subtle signs of cognitive impairment. Some possible signs of memory loss and cognitive impairment include poor recall of recent events, medication nonadherence, change in performance of activities of daily living, and missed appointments.

It is important to distinguish probable dementia from normal cognitive aging, which is characterized by certain cognitive changes, such as speed of information processing and retrieval, that tend to occur with increasing age. At times distinguishing between normal cognitive aging and early dementia can be challenging. It may be helpful to view memory loss over a continuum spanning from normal aging to dementia, with mild cognitive impairment (mild neurocognitive disorder [NCD]) somewhere in between the two ends of the memory spectrum.

Gathering information effectively about deficits is the first step to identify a possible problem.

NW-CALMS is a mnemonic that can help collect and organize the history and background of the patient's memory loss.

- What is the *nature* of the change in memory/cognition?
  - Memory: retrograde memory loss, anterograde memory loss, short-term memory loss, long- term memory loss
  - Language: expressive language, receptive language, anomia

  - Visuospatial: problems with pattern recognition, getting lost in familiar places
  - Executive functioning: planning and sequencing, managing finances, affairs

- *When* was the change in memory/cognition first observed?
  - Onset: when was the last time the person was perceived to be at his/her usual level of cognitive functioning?
- What is the *Course* of the change?
  - Fluctuating, intermittent vs gradual progressive vs rapidly progressive cognitive decline
- Has there been any change in performance of *activities* of daily living (*ADLs*)/instrumental activities of daily living (IADLs)? (see Chap. 3)
  - Be sure to differentiate between functional decline secondary to cognitive impairment from other causes of functional impairment (e.g., stroke with residual weakness that prevents independence with ADLs or IADLs)
- Has there been any recent change in *life situation*, *mood*, or *status* of health?
  - Must rule out potential confounding factors that can impact cognitive function, such as recent illness, depression, and major life changes (e.g., loss of loved one)

If possible, obtain collateral information from family and friends of patients as they may be able to provide additional information regarding onset of memory loss and type/extent of deficits. In some cases these key contributors may be the initial source of information when patients may not be aware of their deficits [2].

Any patient with possible cognitive impairment must be assessed for potential confounders such as depression. The following are useful tools that have been validated to identify depression in the primary care setting: the Patient Health Questionnaire (PHQ) and the Geriatric Depression Scale (GDS). The Physician Health Questionnaire (PHQ) 2 is

often used in primary care settings as a quick assessment for depression [3]. If the patient screens positive for either question, then complete the PHQ-9 (PHQ-2 plus 7 additional questions). Of note, cognitive status should be considered when using the PHQ as a depression screener due to decreased specificity in geriatric patients with cognitive impairment.

The Geriatric Depression Scale (GDS) [4] is another screening tool that has been validated in older adults. The GDS is formatted with Yes/No questions which may be easier for some patients. These screening tools can be administered in various ways to fit the patient and the practice. The tools can be sent in the mail prior to the visit for the patient to complete. Alternatively, the patient can be assisted by a nurse or other staff member asking the questions and completing the screening tool, or the patient can try to complete on his/her own during the visit, and the provider can review with the patient.

Cognitive assessment screening tools are critical in the assessment of cognitive function [5]. The following are validated tools that are easily used in a primary care setting (Table 35.1).

These are screening tools only with general score cutoffs regarding cognitive functioning. However, changes in the patient's functional status must be considered when evaluating a patient for cognitive impairment. For rare cases where there is incongruence between functional status and assessment performance (e.g., MoCA score of 13 with full independence in ADLs and IADLs), further neuropsychological testing could be warranted.

Neuroimaging is often obtained during the evaluation of cognitive impairment [9]. Computed tomography (CT) scan of the brain without contrast is typically the first imaging completed in the primary care setting. It provides a general view of brain anatomy. It can detect generalized atrophy, space-occupying lesions, and previous large territory infarcts and can visualize subdural hematoma and stroke.

Magnetic resonance imaging (MRI) of the brain without contrast is more specific and can give information on cerebral brain volume, specific areas of atrophy (i.e., hippocampal in Alzheimer's Disease), white matter changes, and smaller infarcts (i.e., vascular dementia, mixed dementia).

TABLE 35.1 Cognitive screening tools

Screening tool	Time to administer	Domains tested	Scoring	Sensitivity/specificity in detecting dementia	Advantages (A)/ disadvantages (D)
Mini-Cog [6]	~3 min	Memory, construction	Total score = Word Recall score (3 possible points) + Clock Draw score (2 possible points). A total score of 3 or greater indicates lower likelihood of dementia but does not rule out some degree of cognitive impairment	Sensitivity, 99% Specificity, 93%	A: quick screening tool D: some individuals with clinically meaningful cognitive impairment will score within normal limits

(continued)

TABLE 35.1 (continued)

Screening tool	Time to administer	Domains tested	Scoring	Sensitivity/specificity in detecting dementia	Advantages (A)/ disadvantages (D)
Mini-Mental State Examination (MMSE) [7]	7–10 min	Orientation, attention, comprehension, memory, language, construction	A MMSE score of less than or equal to 23 is generally accepted as indicating cognitive impairment	Sensitivity, 84% Specificity, 78%	D: poor sensitivity in MCI (minimal cognitive impairment) and difficulty detecting changes in severe dementia
Montreal Cognitive Assessment (MoCA) [8]	10–15 min	Executive function, visuospatial, naming, memory, abstraction, language, attention, orientation	A MoCA score equal to or less than 25 is generally agreed on as being suggestive of cognitive impairment	Sensitivity, 87% Specificity, 100%	A: increased sensitivity in diagnosing MCI. Available in multiple languages D: time to administer so usually not done in primary care

Further evaluation for abnormal metabolism/activity is typically reserved for differentiating between types of dementia and not used for routine diagnosis. In the appropriate patient, the positron emission tomography (PET) scan or fluorodeoxyglucose PET (FDG-PET) scan can be used. PET identifies areas of reduced brain activity. FDG-PET directly measures brain metabolism by measuring glucose update by parts of brain (decreased uptake in temporal and parietal areas in AD and decreased uptake in frontal and temporal areas in frontotemporal dementia).

Differential Diagnosis

Various medical, neurologic, and psychiatric conditions can affect memory and cognition. Practitioners must approach the initial evaluation of memory loss with a broad differential as it can be the presenting symptom of a variety of conditions. The following conditions may present with memory change:

- Depression
  Elderly patients with depression may present with a syndrome of cognitive impairment resembling dementia that subsides after remission of depression [2]. Therefore, it is necessary to screen for depression and treat if present as it may be a reversible cause of the cognitive impairment (previously described as pseudodementia).
- Delirium
  Delirium is defined as an acute alteration of consciousness, characterized by inattentiveness which can often present as memory loss. Delirium typically has a reversible cause (e.g., infection), but even after identifying and addressing the cause, delirium can persist for days, weeks, or months before complete resolution occurs. Delirium can present with hyperactive and hypoactive forms. Recognition is critical as there is an increased risk of morbidity and mortality with delayed diagnosis and treatment. Patients with underlying dementia are at increased risk for delirium, so

it is important for patients to be screened for cognitive impairment once delirium has resolved [2].

- Normal Pressure Hydrocephalus (NPH)
  In this condition patients may present with a triad of urinary incontinence, memory loss, and falls [10]. Neuroimaging shows enlarged ventricles. With lumbar puncture there may be an improvement in symptoms but possibly incomplete resolution of memory symptoms.
- Hypothyroidism
  Thyroid-stimulating hormone (TSH) should always be checked in the initial evaluation of patients with cognitive impairment as hypothyroidism, and hyperthyroidism can cause symptoms of cognitive impairment [11].
- Vitamin B12 Deficiency
  Memory loss related to B12 deficiency can present with or without neuropathic complaints or hematological abnormalities. Vitamin B12 levels should be checked in the initial evaluation of cognitive impairment [12].
- Sleep Impairment or Related Disorders
  Insomnia can be associated with cognitive decline [13], and untreated obstructive sleep apnea (OSA) can also present with symptoms of MCI or dementia [14].
- Medication Side Effects
  There are many medications associated with somnolence or that have anticholinergic side effects and may cause cognitive impairment. These medications are commonly found on BEERS list which is a regularly updated list of medications considered to be inappropriate or to be used with caution in the elderly [15]. Clinicians must always consider polypharmacy as a possible cause of cognitive problems or delirium. Psychoactive medications and drug–drug interactions may result in forgetfulness or confusion.
- Mild Cognitive Impairment (MCI)
  MCI is noted as mild neurocognitive disorder in DSM-V [16]. With MCI, there is decline in memory and cognition, objectively demonstrated via testing, but without functional impairment and therefore no impact on patient

independence. It is further classified as amnestic (significant deficits in short-term memory) or nonamnestic MCI. Patient with MCI can revert to normal cognition (rare), remain stable for years, or progress to dementia [17]. There is an increased risk of progression to AD if the patient has amnestic MCI.

– Dementia (Table 35.2)

Treatment

Medications (Table 35.3)

Clinical Pearls

– Patients with depression can present with memory loss. Treating depression may result in reversal of memory loss, but depression can also coexist with mild cognitive impairment or dementia.
– Sleep disturbances can impact cognition and present as memory loss.
– Be cautious of diagnosing mild cognitive impairment or dementia in the acute hospital setting as presentation could be confounded by delirium. With resolution of delirium (days to months), patient should be screened for cognitive impairment.
– Diagnosis involves assessment of subjective (patient and collateral information) and objective (cognitive screening tools) information in the context of the patient's functional status.

Don't Miss This!

– Review medication list for drugs that can impair cognition.
– Assess for mood disorders, delirium, and sleep disorders.
– Screen for hypothyroidism and B12 deficiency.

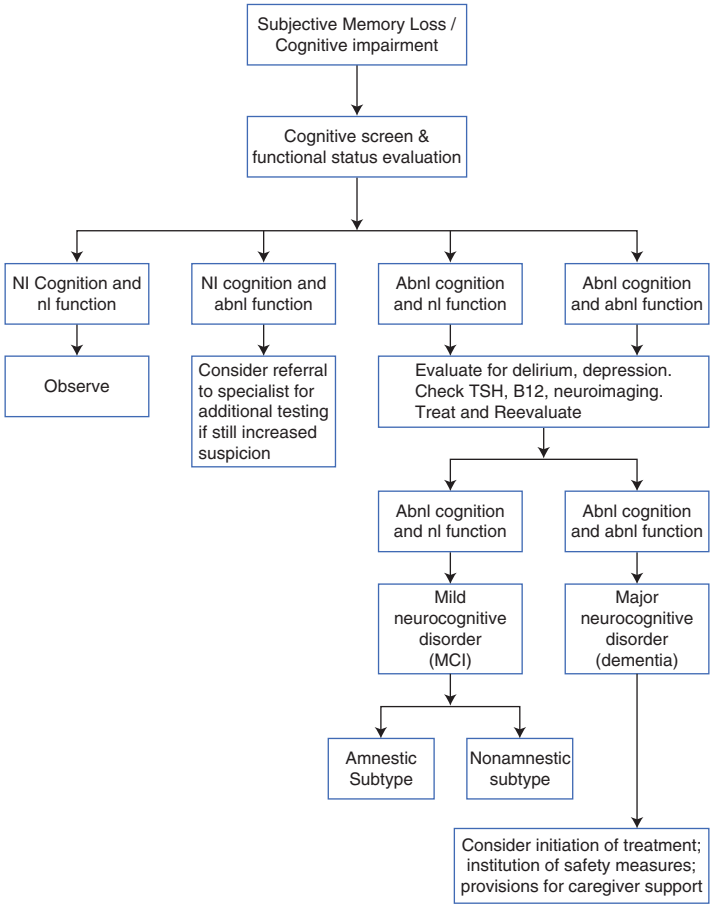

FIG. 35.1 Memory loss evaluation algorithm

– Look for coexisting movement disorders (tremor, bradykinesia, shuffling gait) during the physical exam. Be sure to document timing of onset of movement disturbances in relation to onset of memory complaints (differentiating Parkinson's disease, dementia, and Lewy body dementia).

TABLE 35.2 Dementia (DSM-5: major neurocognitive disorder [16])

Type of dementia	Key fact	Temporal course	Neuropathology
Alzheimer's disease	Most common form, 50–60% of cases	Gradual onset of symptoms, primarily memory loss	Cortical atrophy, hippocampal atrophy, tau protein
Vascular	Second most common. Common in patients with vascular risk factors	Commonly abrupt onset and stepwise progression, but can be slowly progressive with small vessel disease	Ischemic, hemorrhagic, or hypoxic lesions
Parkinson's dementia	Typically have features of parkinsonism	Parkinson's disease for many years prior to onset of cognitive decline	Neuronal loss in the substantia nigra
Lewy body dementia	Typically patients have visual hallucinations, REM sleep behavior disorders early in course	Cognitive complaints appear before or around same time as movement disorder symptoms	Lewy bodies
Frontotemporal dementia (FTD)	Typically earlier onset (<65 years old)	Marked personality changes. Multiple forms including behavioral variant, semantic, progressive nonfluent aphasia, and FTD with motor neuron disease	Tau protein

Other less common forms: alcohol-related dementia, HIV dementia, Prion/Creutzfeldt–Jakob disease, Huntington's disease

TABLE 35.3 Medications

Drug class	Mode of action	Agents/dosing	Common side effects
Acetylcholinesterase inhibitors	Acts at the synaptic cleft by reversibly inhibiting acetylcholinesterase, thereby increasing levels of the neurotransmitter acetylcholine	Donepezil—5 mg daily × 4 weeks, titrate to 10 mg daily Galantamine—4 mg BID (or 8 mg extended-release [ER] daily) for 4 weeks, titrate to 8 mg BID (or 16 mg ER daily long-acting) for 4 weeks, then 12 mg twice daily (or 24 mg ER daily long-acting) Rivastigmine—1.5 mg BID for 4 weeks, titrate to 3 mg twice daily for 4 weeks, then 4.5–6 mg twice daily *or* rivastigmine (Exelon) transdermal 4.6 mg/24 h patch daily for 4 weeks, titrate to 9.5 mg/24 h daily patch, then 13.3 mg/24 h daily patch	Gastrointestinal intolerance (nausea, vomiting, diarrhea, anorexia), bradycardia, and vivid dreams
NMDA-receptor antagonist	Blocks glutamate at NMDA-receptor	Memantine—Start 5 mg daily for 1 week, then 5 mg twice daily for 1 week, then 10 mg every morning and 5 mg at bedtime for 1 week, and then 10 mg twice daily *or* Memantine (Namenda) XR 7 mg every AM for 1 week increasing by 7 mg/week to max dose of 28 mg every AM	Confusion, drowsiness

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