Clinical Evaluation of Early Cognitive Symptoms

J. Riley McCarten, MD

KEYWORDS
- Cognitive • Dementia • Memory • Executive • Alzheimer

KEY POINTS
- An informant (spouse, family member) who knows the patient well is essential to obtaining the history.
- The onset, course, and nature of symptoms are the most important determinants of the etiology of cognitive impairment.
- Standard mental status tests are useful in clinic, but none are diagnostic. The physician must have a good understanding of basic cognitive functions.
- Targeting high-yield aspects of the neurologic examination allows an efficient evaluation and contributes to the differential diagnosis.
- The patient should be present throughout the process of taking the history and providing a diagnosis.

INTRODUCTION

Evaluating symptoms of cognitive impairment shares the basic elements of evaluating symptoms related to other complaints. The onset, course, and nature of symptoms are key to the history and dictate the essential features of the examination. Although it is important to allow patients/informants to describe symptoms in their own words, it is essential that the physician clearly understands the symptoms from a medical perspective. Furthermore, it is crucial that important questions relevant to the etiology of symptoms are addressed. Just as for headache, chest pain, nausea, or dizziness, the investigation of cognitive symptoms needs a combination of open-ended and directed questions to elicit the critical features of the history.

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E-mail address: mccar034@umn.edu

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Evaluating cognitive symptoms, however, does pose challenges not common to other symptoms. Cognitive functions are by far the most complex of biological functions. Symptoms of neocortical dysfunction can be challenging for experts to describe, much less the layperson. Patients often do not recognize the nature or severity of cognitive symptoms, and may be defensive. Family and/or providers may minimize the patient’s symptoms for a variety of reasons: Challenging the integrity of one’s cognitive function may seem disrespectful, particularly if the investigation is uninvited. Cognitive symptoms increase with age and may be seen as an inevitable part of aging, are difficult to assess, and the evaluation may be unsatisfying. Lastly and most importantly, even moderately demented patients, several years into a progressive dementia, may appear cognitively normal during a typical office visit. This fact cannot be overstated. Primary care physicians overlook cognitive impairment far too often.\textsuperscript{1,2}

Though challenging, a structured approach to the evaluation of cognitive symptoms should provide the information needed to make informed clinical decisions in the best interest of patients, caregivers, and providers.

The foregoing describes the clinical evaluation in a medically stable outpatient. The diagnosis of a progressive, irreversible cognitive disorder should not be made in an acutely ill or stressed older adult. Conversely, awareness of underlying cognitive impairment can prepare providers, family, and the patient for the commonly seen exacerbation of cognitive symptoms when illness and stress do occur.

**THE INTERVIEW**

**Overview**

When the patient presents with cognitive complaints, or when problems are suspected during the course of the interview or examination, it is best to have a knowledgeable informant available. Often this informant is in the waiting room. Because cognitive problems are so common in the elderly, it is reasonable to ask any unaccompanied older patient if he or she came with anyone, and if it would be permissible for that person to join the interview. The request is rarely denied.

If the patient is truly alone and cognitive symptoms are suspected, do not waste time with a potentially unreliable history. Rather, move directly to mental-status testing. If deficits are identified, the time saved can be used to identify an informant and review the history. Problems identified in the course of a visit not specifically for cognitive symptoms usually will require a separate appointment.

Symptoms of cognitive impairment often are intertwined with complex psychosocial issues. When dementia is clearly present, cognitive impairment is readily recognized as a contributing factor. When cognitive impairment is mild or questionable, it may be difficult to identify the difference between symptoms caused by brain disease and those related to anxiety, depression, medications, or situational factors. Patients and families often have their own ideas about cause, and may offer elaborate but tangential examples to support their viewpoints. Conversely, patients or, more often, families may be reluctant to discuss sensitive issues. It is important, therefore, that the physician establish the ground rules for the interview process to promote an efficient and thorough assessment.

**Setting the Ground Rules**

When taking the history from more than 1 person (eg, a patient, spouse and/or adult children), the patient and family members should be seated next to each other, not across from one another. The physician should be able to see the reactions of family members to the patient’s answers, and responses from family members often are
guarded when the patient is looking at them. Family members also may try to coax or coach the patient’s responses. Not only is it easier to maintain control over the interview if the physician can see the patient and all family members at the same time, more information, often unspoken, is also gleaned.

**Interviewing the Patient**

The interview may be introduced by saying to the patient, “First I’d like to ask you some questions and then, if it is OK with you, I’d like to ask your [family] some questions.” This request is rarely denied. It gives the patient the first chance to express concerns and promotes establishment of the doctor-patient relationship. Begin with an open-ended question to the patient, such as “Why are you here today?” If the appointment is specifically to address cognitive symptoms, the answer may reveal important information about the patient’s insight. If the patient does not volunteer cognitive complaints, ask specifically “How is your memory?” “Memory” in lay terms typically covers a broad range of cognitive deficits. If deficits are acknowledged, ask the patient how long he or she has been aware of it, and if it causes problems. Ask if the patient feels clear-headed or confused, which may suggest delirium. Ask about mood and general health. Usually this entire interview with the patient is brief.

Do not let family interrupt when interviewing the patient, or let the patient defer to the family, noting, “They’ll get their chance.” Such interruptions or deferrals are telling, but it is also important for the physician and family to hear what the patient believes the problem to be. It may be useful to reiterate for the patient what you have heard.

**Investigating the Family**

With the patient’s permission, which is almost invariably granted, direct further questions to the family/informant. An important first inquiry is to establish the frequency of contact the family member has with the patient. Sometimes the family member sees the patient infrequently or has reestablished ties only recently. If someone who knows the patient well did not attend the visit, find out why. Such information may not be volunteered but obviously is important.

**Onset and Course**

Ask of the informant, “Does [the patient] have a [cognitive] problem?” If yes, the onset and course are critical to establishing a cause. Often, family members wish to emphasize recent changes that have prompted the current evaluation. Slowing evolving changes that have caused problems in the recent past are very different from acute or subacute changes that truly began only recently. A useful question is, “When was the last time [the patient’s] thinking and memory was 100%?” Disregard reported age-related changes. Patients and families, and often clinicians, may want to attribute changes to “normal aging,” but such changes are rarely evident outside of a formal neuropsychological assessment. Older adults are expected to manage complex medications, finances, and social relationships. Many are fully engaged in demanding careers. Changes resulting from disease are much more often attributed incorrectly to “normal aging” than are changes of normal aging attributed incorrectly to disease.

**The Major Causes of Brain Disease**

The major causes of brain disease tend to have characteristic onsets and courses: vascular events (stroke) and head trauma are acute; infectious/inflammatory conditions are subacute, usually evolving over hours to days and, rarely, weeks; neoplasms are subacute, but typically evolve over weeks to months; toxic/metabolic conditions are usually subacute, also over weeks to months, and fluctuate with the underlying
cause; and degenerative brain disease has an indolent but inexorably progressive course, with symptoms typically apparent for a year or more before an evaluation. Because families often report changes as sudden, a useful question is, “Have you ever thought he/she was having a stroke?”

**Neurodegenerative Diseases**

Neurodegenerative diseases, primarily Alzheimer disease (AD), but also diffuse Lewy body disease (LBD) and frontotemporal dementias (FTDs), are the major causes of cognitive disorders in older adults (Box 1). If symptoms are progressive but only gradually so, the longer ago they began, the more likely the primary underlying etiology is neurodegenerative. When the onset is ambiguous but claimed to be recent, look for evidence that symptoms were present further back in time. Clues include mistakes in the patient’s management of his or her job, finances, medications, or other instrumental activities of daily living (IADLs; ie, the ADLs beyond basic self-care that are needed to function independently). The further back in time the symptoms began, the more likely the origin is neurodegenerative disease.

**Nature of Symptoms**

The nature of symptoms provides other important clues to the etiology of cognitive impairment, and directed questions may be most useful for this purpose (Box 2).

<table>
<thead>
<tr>
<th>Box 1</th>
<th>Common dementias and their frequencya</th>
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<tbody>
<tr>
<td>1. Alzheimer disease (60%–80%)</td>
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<tr>
<td>2. Diffuse Lewy body disease (5%–10%)</td>
<td></td>
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<tr>
<td>a. Dementia with Lewy bodies</td>
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<tr>
<td>b. Parkinson disease dementia</td>
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<tr>
<td>c. Multiple system atrophy</td>
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<tr>
<td>3. Frontotemporal dementia (FTD) (12%–25%)b</td>
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<tr>
<td>a. Behavioral variant</td>
<td></td>
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<tr>
<td>b. Language variant</td>
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<tr>
<td>i. Primary progressive aphasia—expressive aphasia</td>
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<tr>
<td>ii. Semantic dementia—receptive aphasia</td>
<td></td>
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<tr>
<td>c. Motor variant</td>
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<tr>
<td>i. Progressive supranuclear palsy</td>
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<td>ii. Corticobasal degeneration</td>
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<td>iii. FTD with parkinsonism</td>
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<tr>
<td>iv. FTD with amyotrophic lateral sclerosis</td>
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<tr>
<td>4. Vascular dementia (10%–20%)c</td>
<td></td>
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<tr>
<td>5. Mixed etiology (10%–30%)</td>
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*a Overlapping abnormalities are common.

*b Most FTD is young onset, <65 years old.

*c Vascular dementia is not consistently defined. In the absence of significant strokes involving gray matter, the contribution of cerebrovascular disease to cognitive impairment is speculative.

Data from Refs.7,19,20
### Box 2
### The history

- Set the ground rules
  - Patient and family members next to—not across from—each other
  - Begin with patient but keep it brief. Do not allow family to interrupt
  - With the patient's permission, direct questions primarily to family
  - Patient should be present throughout
- Define onset and course of cognitive symptoms
  - When was the patient last completely normal?
    - Disregard “normal aging”
    - Onset is not when “things got bad”
  - Have symptoms progressed and, if so, gradually or suddenly?
    - Have you ever thought the patient was having a stroke?
- Define nature of cognitive symptoms
  - Memory:
    - Repeating?
    - Misplacing?
    - Relying more on notes/calendars?
    - Forgetting names of familiar persons?
  - Language:
    - Trouble finding words?
  - Visuospatial/executive function:
    - Lost driving or other driving issues?
    - Mistakes with medications or finances?
    - Difficulty with former skills?
      - Preparing a meal
      - Household repairs
      - Using tools/appliances
    - Safety concerns?
- Address associated behavior changes
  - Depressed, anxious, agitated?
  - Personality change?
    - Impulsive, inappropriate
    - Loss of empathy
  - Visual hallucination?
  - Paranoia?
  - Sleep disruption?
  - Involuntary movements or gait disturbance?
Families and mildly impaired patients typically recognize symptoms with little or no explanation from the examiner. Does he or she misplace? Struggle with names of familiar persons? Rely more on notes and calendars? [typically reflecting memory deficits] Get lost driving? [memory or visuospatial deficits] Have trouble finding words? [language deficits] Of course, all of these symptoms must reflect a decline from an earlier baseline.

Patients are rarely aware of repeating themselves (a typical symptom even early in the course of AD), but families typically readily recognize the simple question, “Does he/she repeat?” Frequent repetition of questions, often verbatim by the patient, can be exasperating for families.

Inquiries directed at executive functioning can be challenging. Executive functions refer to skills typically localized to the frontal lobes and involve organizing, planning, execution, and judgment. The ability to sequence, shift sets, and multi-task are all dependent on executive functions, and deficits may cause difficulty preparing a meal, completing a household repair, or preparing financial documents. Perhaps fortunately, executive dysfunction is often misinterpreted as a memory problem, because patients appear to have forgotten how to do things. Executive deficits are common in dementia, including AD, and are the hallmark of FTDs. A simple question that may encompass executive dysfunction is, “Do you have safety concerns [for the patient]?”

Remarkably, despite the ready endorsement by families of many or all of the cognitive deficits described, it is often a surprise to them that the patient may have trouble managing medications or finances. Even more remarkable, patients who are acknowledged to be dependent on others for virtually all IADLs, and even those needing assistance with basic ADLs, are thought by family to be safe drivers. Often, no family members have ridden with or observed the patient’s driving.

Although it is important to return to driving or to other issues that relate directly to the patient’s independence, do not let these matters sidetrack the evaluation.

**Investigating Behavioral Symptoms**

Behavioral changes are universal in brain disorders that cause cognitive impairment. Asking the family about the patient’s mood is important, but one must be aware that vegetative signs reflecting apathy, not depression, may accompany even early symptoms of dementia. It may take a skilled geropsychiatrist to differentiate the apathy of dementia from true depression that often accompanies dementia. Older adults with cognitive disorders may improve significantly with treatment of their comorbid mood disorder, but depression, anxiety, mania, and other psychiatric conditions rarely develop as a primary disorder in late life. Even in the absence of overt cognitive impairment, such patients should be watched for an evolving neurodegenerative disorder.

**Personality Change**

Many changes in behavior may be interpreted as a personality change, but true personality change, characterized by impulsive, odd, and inappropriate behavior, apathy and indifference, or coarsening of affect with loss of empathy are hallmarks of behavioral variant FTD and also can be seen in traumatic brain injury (TBI). Such patients may appear quite normal in the clinic and may test well on structured mental-status examinations. Often, only the people who know them best recognize the change. When the patient appears normal and the family appears distressed, think frontal lobes.

**Hallucinations and Delusions**

Visual hallucinations are relatively specific to LBD (synucleinopathies), particularly early in the disease course, and should be asked about in all older adults with...
suspected cognitive impairment. Auditory hallucinations are much less specific and are not common in the early course of dementia. Delusions, which are common in dementia, may be reported by the family as hallucinations based on the patient’s statements of having seen or heard things. Confirm that family members have observed the patient hallucinating and are not just reporting what the patient has said.

Patients may be more prone to misinterpret sights or sounds (illusions), sometimes attributing a threatening quality to them. Forgetfulness and impaired judgment also can trigger paranoid delusions and may prompt accusations of stealing or other bad behavior. Pleasant delusions, such as the patient believing he or she recently visited with a long-dead friend, also may occur and, while sometimes upsetting to families, are not harmful and may actually offer opportunities to engage the patient in conversation.

**Sleep**

Sleep changes are common in older adults, and disrupted sleep can exacerbate cognitive symptoms. However, it is uncommon for sleep disorders to be the primary cause of cognitive impairment. The treatment of sleep apnea, restless legs, or other disorders causing excessive daytime sleepiness can improve attention but rarely eliminates the perceived changes in cognitive impairment. Rapid eye movement behavior disturbance, a sleep disorder characterized by often dramatic motor activity accompanying vivid dreams, is suggestive of LBD, as are visual hallucinations.

**Motor Disturbances**

Involuntary movements and/or a gait disturbance may suggest LBD, a motor variant FTD, or, in another context, a toxic encephalopathy (delirium). Lateralized weakness or numbness may suggest focal brain lesions, such as stroke, subdural hematoma, or TBI. Bowel or bladder disturbance or symptoms of presyncope may indicate dysautonomia, also seen in LBD (multiple system atrophy).

**The Past Medical History**

A complete medical history is important, with particular emphasis on prior neurologic or psychiatric problems. In general, the brain is a resilient organ which, given enough time, can compensate for significant impairment to other organs. Apart from end-stage pulmonary, cardiac, hepatic, or renal disease, patients have at least intermittent mental clarity.

**Medications**

A review of medications with special attention to adherence and to drugs with central nervous system activity, including over-the-counter and illicit drugs, is important. Stable doses over years of benzodiazepines, opiates, antiepileptic drugs, or even alcohol are not likely to present as a progressive cognitive impairment unless blood levels are increasing and/or tolerance is decreasing. Not infrequently, patients with cognitive impairment make medication errors. In addition, common behavioral and psychological symptoms of dementia may lead to self-medication with drugs or alcohol.

**The Family History**

The family history is important, particularly if there is a strong history of mid-life neurodegenerative disease. The vast majority of dementia is sporadic, and late-life dementia in a relative condones only a mild increase in risk. Nevertheless, it is often a concern that prompts the patient to seek an evaluation.
The Social History

The patient’s education, occupation, current activities and hobbies, home life, social support, and belief systems are all important factors that influence the presentation of cognitive symptoms.

The Review of Systems

Though often mandatory, the review of systems from an unreliable historian is virtually worthless. A standard form that the patient can review with a knowledgable family member before the visit to the clinic is preferred.

Interviewing the Family Separately

Although families often want to speak to the physician independently, it is best to address issues of cognitive impairment as openly and honestly as possible with the patient present. Beyond the ethical issues, deceiving or withholding information from the patient may sabotage the doctor-patient relationship. Patients may be forgetful, but they usually recognize whom they trust. Moreover, when families are reluctant to speak in front of the patient, the patient typically has limited insight and fairly significant cognitive impairment. In such situations, families are usually unduly concerned about what the patient will remember. The patient often is indifferent or, if upset, has a short-lived irritation. For patients who are more mildly or even questionably impaired, there is rarely justification for discussing concerns with the family without the patient being present.

The process of diagnosing dementia may be stressful for patients, families, and physicians, but trying to spare patients from potentially bad news is a poor strategy for managing any disease. Usually, when the physician is straightforward families do not feel the need to speak apart from the patient, and both patient and family are grateful for the physician’s honesty.

The Examination

Background

Although a general medical examination is important, the neurologic examination is key to diagnosing cognitive impairment. Observations about the patient’s psychological state, including mood, affect, character of speech, thought content, and insight may influence the assessment, but in the cooperative and attentive older adult, cognitive impairment usually can be detected unless psychiatric symptoms are extreme.

The Neurologic Examination

The neurologic examination uses a carefully constructed approach to localize lesions within the nervous system. Findings are addressed in a deliberate fashion, beginning at one end of the neural axis (brain cortex) and sequentially adding considerations of other nervous system components. The mental status, reflecting function of the cerebral hemispheres, is considered first. The cranial nerves add a consideration of the brainstem. The motor examination adds the spinal cord, efferent nerves, neuromuscular junction, and muscle. The sensory examination adds afferent nerves and ascending spinal cord pathways that eventually relay in the thalamus and project to cortex. Lastly, coordination, station, and gait testing adds a consideration of cerebellar and basal ganglia input, which work through the motor system and depend on sensory feedback.
Localizing Cognitive Functions

In the alert (eyes open) and attentive (maintains eye contact) adult, the major spheres of cognition are memory, language, and visuospatial and executive function (Fig. 1). Each localizes to important brain regions.

The critical structures for making new memories are the hippocampi, deep in the medial temporal lobes. Language localizes to the dominant (usually left) temporoparietal cortex, visuospatial function to a similar region of the nondominant hemisphere, and executive function to the frontal lobes (Fig. 2). Note that language, visuospatial function, and executive function are neocortically based, whereas memory depends on the much more primitive archicortex of the hippocampus. Neocortical deficits may be difficult to identify in the clinic, particularly in a well-educated patient. Recent or “short-term” memory, the crucial ability to learn and remember new information, tends to be easier to test and is usually affected first and foremost in AD.

Orientation is not useful for localization, is not sensitive to cognitive dysfunction, and has no uniformly recognized criteria. If a patient presents at the correct time and place, little is gained by quizzing orientation.

The Mental-Status Examination

The initial mental-status examination should be administered in a rigorous fashion, ideally by a nurse or other support staff trained in the administration of standard tests. Many such tests are available.10,11 If there is no reason to expect cognitive dysfunction, a brief (~2 minutes) screen, such as the Mini-CogTM,12 is adequate. If problems are suspected, a more extensive test, such as the Montreal Cognitive Assessment

Fig. 1. Structures that are midline and deeper in the brain are more primitive. After recovery from an acute, bilateral insult to the brain (eg, anoxia), alertness requires only the reticular activating system. Attentiveness requires thalamic drivers to keep the cortex in a receptive state. Recent or “short-term” memory is dependent on the hippocampi, a primitive archicortex. Language, visuospatial, and executive functions are all more evolved, depend on the neocortex, and may be difficult to assess in a brief examination.
MoCA,13 can be used. The scores on such tests are not diagnostic but do alert the physician to the potential need for further evaluation.

It is essential for the physician to have a good working knowledge of cognitive function to help decide if (1) the patient is a reliable historian and responsible partner in recommended care; and (2) further testing is needed and, if so, what.

Families should be invited to observe the mental-status examination. Not infrequently, they are shocked at the patient’s performance.

**Recent Memory**

Because of its importance to the history and treatment recommendations, it is imperative that the recent or short-term memory be assessed. A patient with impaired recent memory is, de facto, an unreliable historian and also should not be accountable for adhering to treatment recommendations, including medications. Just as with any other abnormal examination finding, the physician should reassess recent memory as needed until he or she is convinced that there is or is not a problem.

Recent memory is tested by delayed recall. Most commonly the patient is asked to remember 3 unrelated words and to later recall the words after an interference (distracter) task. Not all words lists are equal,14 and a standard list, such as “leader, season, table” should be used. The interference task, not the time delay, is key to identifying deficits in recent memory and must be adequately demanding to fully engage the patient. Common interference tasks include serial 7 subtractions (“Count backwards from 100 by 7s”) and reciting the months of the year in reverse order, either of which is also a good test of attention/concentration. The clock draw task, the interference task used in the Mini-Cog, assesses visuospatial and executive function (see later discussion).

If a patient struggles to recall the 3 words after the first interference task, have the patient repeat them again, do another interference task, and again test recall. Struggling a second time is concerning. Struggling a third time, again rehearsing the words and using a different interference task, is very likely not normal. The test can be refined by providing letter or category cues, then multiple choice if needed. Patients who do
not recall the words but readily get them with a simple cue (eg, “Starts with the letter,” “A piece of furniture”) may be intact, particularly if they later recall the words without cues. Patients who cannot recognize the words from a multiple-choice list (eg, “sugar, sailor, or season,” or “chair, table, or sofa”) are most concerning, particularly on repeated testing.

Well-educated patients may be able to bear down enough to appear intact on a simple quiz, but deficits may be revealed on their knowledge of current events. Major recent events, such as elections and natural catastrophes, or historic events, such as 9/11, should be recalled by anyone who acknowledges following the news. Mistakes, particularly when unrecognized by the patient, may be startling.

Language

Even when word-finding difficulties are reported, they may not be apparent when talking with the patient. Asking the patient to follow multiple step instructions—essentially, 3-stage commands—is a simple test of comprehension and can be incorporated into most examinations. Be deliberate in giving the patient multiple instructions at once, without cues, as opposed to a series of 1-step instructions. For example, say, “Hold your hands straight out in front of you, elbows straight, palms up, at shoulder level, and close your eyes” [instructions for testing drift]. Decide what is important for any routine examination and invent a way to incorporate a multistage command into that examination. This approach represents an efficient use of time and reveals something of the patient’s likelihood of being able to follow advice.

Generative Naming

Generative naming may be revealing, even when conversation and comprehension appear intact. Semantic (category) fluency tends to reflect temporal lobe functions, whereas phonemic (letter) fluency taps into frontal lobe function. Patients are given 1 minute to generate as many names, typically animals, or words beginning with a specific letter, typically f, a, or s. Jot down the starting time to the second, as tracking words can be demanding. Normally patients generate at least 11 words per minute. Patients with AD may have more difficulty with categories, whereas FTD patients may have trouble with letters.

Naming objects is difficult to qualify and quantify in the clinic, and may be intact until deficits are relatively severe. It is also less revealing than difficulties following instructions or generating words.

Be aware that intact language skills do not preclude significant deficits in memory, visuospatial function, or executive function. Often, even severely cognitively impaired patients appear normal because of preserved language and social skills, basically “talking a good game,” and fooling both family and providers.

Visuospatial Skills

Visuospatial skills are difficult to test in the clinic, despite the profound impact such deficits may have on function. Their assessment often overlaps with that of executive function. Copying intersecting pentagons, in which 2 5-sided figures form a 4-sided intersection, or copying a cube such that the figure appears 3-dimensional, the appropriate lines are parallel and of equal length, and no lines are added, are relatively specific bedside tests for visuospatial deficits.

Executive Function

Executive functions are the most evolved and complex of biological functions in the known universe. Almost half of the brain—the frontal lobes—is dedicated to executive
These functions also may be most important to successful independent living, because they are the basis of planning, organizing, recognizing patterns, shifting attention as needed, and making sound judgments. Nevertheless, deficits may be difficult to recognize in the clinic. Because they are so involved in interpersonal interactions, it is not surprising that persons who know the patient best may recognize changes before others. Facial expression, body language, and tone of voice may speak volumes to family members but mean little to a relative stranger.

It must be reiterated here that when a patient appears normal and has no complaints, but the family looks distressed, think frontal lobes.

**The Clock-Draw Task**

The clock-draw task taps into both visuospatial and executive functions (planning, abstracting), and is an efficient way to screen for either. There are a variety of ways to score the clock. Basically all 12 numbers should be present, in order, only once, in the correct clockwise direction, and the hands should point to the correct numbers. Ideally the drawing should be well planned, with quadrants defined, numbers correctly spaced, and hands of the appropriate length. The time “11:10” is most often used, the instruction being, “Place the hands at 11:10, 10 minutes past 11.” Impaired patients are often “stimulus bound,” and tend to draw hands pointing to the 10 and 11. Other times, including 8:20 and 1:45, also require abstraction and are only slightly less likely to reveal deficits.

**Sequencing**

Sequencing may be challenging for patients with executive dysfunctions, if not more global cognitive impairment. The Luria sequencing task, or fist-edge-palm test, is administered as follows. Instruct the patient to “Watch me.” Do not provide any verbal cues. Demonstrate the sequence of fist (fingers balled, perpendicular to the floor), edge (hand open, perpendicular to the floor), palm (hand open, parallel to floor), tapping your hand on your thigh as you perform each movement. Use a silent 4-count beat (1 beat rest after each sequence) to clearly distinguish the 3 steps. Perform the demonstration 3 times, and then say to the patient, “Now you do it.” A normal patient performs this readily, 3 times in a row. If the patient does not perform it correctly 3 times, say “Do it with me,” and demonstrate 3 more trials, making sure the patient mimics your hand position. Then say “Keep going.” The test is scored as spontaneously correct, correct with coaching, partially correct (1 or 2, but not 3 correct sequences in a row), or unable to do.

**Set-Shifting**

Set-shifting is another challenging task for persons with frontal lobe dysfunction, and also for those with any significant deficits in attention (delirium). Trails B is a neuropsychological test whereby numbers and letters are randomly distributed on a page and the patient must connect them in the correct, alternating sequence: 1-A-2-B-3-C, and so forth.

Trails B can be administered orally, tapping into executive function, attention, and working memory. Say to the patient, “Complete this sequence: 1-A-2-B-3-C.” Most can complete the entire sequence, arriving at 26-Z or close to it. Those with executive dysfunction often charge ahead but quickly lose track of the sequence, responding incorrectly with all numbers or letters, or sequences that are clearly out of order. Those with even subtle delirium, (eg, mild intoxication or medication side effects) may quickly lose their place. Patients able to complete this task are unlikely to have delirium, and any other cognitive deficits identified are usually the product of brain disease.
The oral Trails B task is also an excellent interference task for testing memory. It is virtually impossible to rehearse newly presented information, thereby enhancing delayed recall, and correctly attend to this task.

As noted under language function, phonemic fluency (the number of words generated in 1 minute beginning with f, a, or s) also tends to be disproportionately impaired in disorders affecting the frontal lobes.

Other clinical assessments of executive/frontal lobe function often have biases and are difficult to quantify, but can be revealing to the experienced clinician. The interpretation of proverbs depends on the patient’s age, culture, and education. The response demonstrating the optimal abstraction is another proverb of the same meaning. Interpreting similarities and differences (eg, how are an orange and a banana alike?) may be complicated by creative responses (both are good sources of potassium).

The Remainder of the Neurologic Examination

The neurologic examination is often seen as overly complex and time consuming, but most findings relevant to the differential diagnosis of cognitive impairment can be gathered in short order (Box 3).

It is much better to make a few valid, reproducible observations than to make generalizations such as “grossly intact,” “nonfocal,” or “nonlateralizing.” Each of the following descriptions of a normal examination take only moments to observe or test, yet are of high yield in terms of assessing the integrity of the nervous system outside of the mental status.

Cranial nerves: Visual fields full, extraocular movements (EOMs) intact, face symmetric, speech articulate, hearing intact to soft voice.

Stands easily from a chair without pushing off, gait normal, walks well on tiptoes and heels, station normal, postural reflexes intact, Romberg negative, Drift negative, finger-to-nose testing and rapid alternating movements intact.

In the most abbreviated neurologic examination, apart from always testing recent memory, the EOMs and the gait are the most important to test. Develop skill in watching for smooth, seamless pursuit movements without evidence of intrusion saccades. The observation of a normal gait, which is readily recognized, may be an invaluable piece of information to document and track.

ADDITIONAL TESTING

Brain Imaging

Frequently, brain imaging (magnetic resonance imaging or computed tomography) is used as a substitute for the neurologic examination. The brain is tremendously dynamic, and a static picture may reveal little about neurologic function. The most common cognitive disorders, namely neurodegenerative dementias, are not evident on routine imaging, and functional imaging is confirmatory at best, not diagnostic. The strongest argument for brain imaging for cognitive impairment is that the patient is typically an unreliable historian, and a significant injury or event may be forgotten. Many “abnormal” findings on imaging are nonspecific (eg, the ubiquitous “small-vessel ischemic disease,” which may or may not represent vascular disease) and of no clinical significance. Imaging does rule out significant cortical strokes, TBIs, tumors, subdural hematomas, and hydrocephalus, any of which could cause or aggravate cognitive symptoms.

Laboratory

Vitamin B₁₂ and thyroid-stimulating hormone are the only laboratory tests that commonly are not already part of the clinical laboratory data. A complete blood count,
Box 3
High-yield neurologic examination findings in the evaluation of cognitive symptoms

Cranial Nerves

- Extraocular movements (cranial nerves III, IV, VI)
  - Rationale: Assesses the most discrete of motor movements, requiring multiple coordinated areas of brain function. Abnormal in:
    - Progressive supranuclear palsy, Parkinson disease
    - Some structural lesions
    - Drug toxicity
    - All brain disease, at least subtly
  - Procedure: “Follow my finger with your eyes”
    - Move finger to extremes of gaze at varying speeds
    - Observe particularly for smoothness of pursuit movements
    - Do not hold finger too close, as difficulty converging (older adults) may produce nonpathologic intrusion saccades (choppy eye movements)
  - Normal: Seamless, conjugate pursuit of target
  - Abnormal:
    - Dysconjugate or lack of full range of motion (mildly limited up gaze in older adults)
    - Significant nystagmus (beyond mild, symmetric end point)
    - Decrease in smoothness of pursuit movements (nonspecific but sensitive)

- Speech (cranial nerves V, VII, IX, X, XII)
  - Rationale: Multiple brain and peripheral structures are involved. May be abnormal in:
    - Bilateral corticobulbar (pseudobulbar) lesions
    - Bulbar (lower brainstem) lesions
    - Basal ganglia and cerebellar disorders
    - Some lateralized structural lesions
    - Drug toxicity
  - Procedure: Assess speech quality during interview
  - Normal: Speech articulate, volume normal
  - Abnormal:
    - Dysarthria (slurred; eg, cerebellar/brainstem lesions, drug toxicity)
    - Hypophonia (eg, Parkinson disease)
    - Halting (eg, basal ganglia, language cortex)
    - Dysphonia (hoarseness)/nasal speech (brainstem or peripheral structures)

Drift

- Rationale: May detect lateralized motor, sensory, cerebellar deficits; highly reproducible
- Procedure: Arms extended, palms up, shoulder level, eyes closed
- Normal: Holds for 10 seconds; tremor is discounted
- Abnormal: One arm
  - Pronates, may also drift downward (corticospinal tract lesion)
  - Drifts laterally to 45° (ipsilateral cerebellar dysfunction)
  - Drifts upward (may be central sensory deficit)
Stand
- **Rationale:** Detects weakness, postural instability that poses risk of falls; highly reproducible
- **Procedure:** Cross arms over chest and stand up
- **Normal:** Patient stands easily without pushing off
- **Abnormal:**
  - Struggles but stands without pushing off
  - Must push off to stand
  - Needs assistance to stand
  - Cannot stand

Gait
- **Rationale:** Requires integrated motor, sensory, basal ganglia, cerebellar function. Gait is often abnormal in:
  - Lewy body disease
    - Untreated Parkinson disease
    - Dementia with Lewy bodies
    - Multiple system atrophy
  - Tau disorders
    - Progressive supranuclear palsy
    - Corticobasal degeneration
    - Other frontotemporal dementias
  - Huntington disease
  - Post–cardiovascular accident or traumatic brain injury
  - Normal pressure hydrocephalus
  - Cerebellar or toxic/metabolic disorders
- **Procedure:** Tell patient, “Take a fast walk down the hall [to bring out abnormalities].” Then, “Come on back [to observe turns].” Note:
  - Base
  - Stride
  - Posture
  - Arm swing
  - Turns
- **Normal:** Walks normally 30 ft down the hallway and returns
- **Abnormal:**
  - Hemiplegic/paretic (lateralized brain lesion)
  - Parkinsonian (basal ganglia, relative dopamine deficiency)
  - Choreiform (basal ganglia, relative dopamine excess)
  - Ataxic (cerebellar; alcohol intoxication causes classic gait ataxia)
  - Magnetic/apractic (normal pressure hydrocephalus and frontal lobe disorders)
  - Neuropathic (peripheral nerve; steppage gait in extreme cases)
  - Myopathic (muscle; may cause waddling with weakness of pelvic girdle)
  - Antalgic (nonneurologic gait disturbance related to pain)
liver and renal function tests, glucose, electrolytes, and calcium should be documented. When appropriate, testing should be done for sexually transmitted disease (rapid plasma reagin, human immunodeficiency virus). The onset, course, and nature of symptoms may dictate further evaluations (eg, Lyme titers, drug and heavy metal screens) but are infrequently indicated and should not be pursued in what appears to be a typical case of AD, LBD, or FTD.

**Neuropsychological Testing**

Formal neuropsychological testing is invaluable when assessing truly mild or questionable symptoms of cognitive impairment. Each of the major domains of cognition already outlined is assessed with multiple, standardized tests. The neuropsychologist with an interest in older adults may be skilled at diagnosing AD versus LBD versus FTD. Not all neuropsychologists have the same skill sets, and some are much less willing than others to endorse a pattern suggesting an irreversible, progressive brain disease. The neuropsychologist may place undue weight on the report of neuroimaging (small-vessel ischemic disease), vascular risk factors, and a history of alcohol use.

**Functional Assessments**

Occupational therapists may be skilled at assessing ADLs and IADLs in older adults. A structured, performance-based evaluation, such as the Cognitive Performance Test,17 has the advantage of allowing family members to observe as patients are directed to perform various tasks. Prompts are provided in a graded fashion until the task is completed, revealing the degree of assistance needed. Such information may be crucial in deciding if the patient has the “impairment in function” that is integral to the definition of dementia, and can be telling about the safety of the patient’s current activities and environment.

**Other Tests**

When indicated, a sleep study should be pursued before neuropsychological testing. An electroencephalogram occasionally is helpful if there is a true question of spells of confusion, or if a subacute progression suggestive of prion disease is suspected.

It is important to recognize that the vast majority of cognitive disorders are clinical diagnoses, and ancillary tests rarely identify a reversible cause.18

**THE ASSESSMENT**

The physician’s first job is to decide if there is: (1) no cognitive impairment; (2) cognitive impairment, not dementia; or (3) dementia. For either of the latter 2 possibilities a specific etiology should be sought, which will directly relate to the prognosis and steer the patient and family to the resources needed.

**REFERENCES**