Neuropsychologic Assessment for Neurodegeneration

What is the value of neuropsychologic assessment in neurodegenerative diseases?

By Jennifer Medina, PhD and Sarah J. Banks, PhD, ABPP-CN

Introduction

Neuropsychology is the science linking brain function with cognition and behavior. Clinically, it is the diagnosis and tracking of cognitive or behavioral symptoms of brain disorders.

Who Is a Neuropsychologist?

Clinical neuropsychologists in the US have doctorates in clinical psychology, either a PhD or a PsyD. Neuropsychologists typically complete specialized training during predoctoral internships and postdoctoral fellowships, making them experts in diagnosis and treatment planning for people with brain disorders. The title neuropsychologist is not protected in most states, which makes it necessary to ensure a provider is well qualified. The American Board of Professional Psychology oversees board-certified neuropsychologists, ensuring training and knowledge assessed via written and oral exams for anyone with the title board-certified neuropsychologist (ie, ABPP-CN). This is a relatively new process, however, and not a requirement for practicing. In many states, there are only a few board-certified neuropsychologists. Fortunately, there are many competent neuropsychologists who are not board certified. Neuropsychologists are often researchers who conduct both observational and interventional studies. The Food and Drug Administration (FDA) requires that a cognitive measure be part of outcomes in clinical trials in Alzheimer’s disease (AD) in all but the biomarker-only stage. Thus neuropsychologists are involved in clinical trial design.

How to Find a Neuropsychologist

Neuropsychologists can be found in a variety of clinical settings. Inpatient work is usually helpful with assessing acute conditions, delirium, or suspected dementia in a person hospitalized for a different reason. Specialized outpatient clinics, such as memory disorders clinics, typically offer multidisciplinary care for AD and related disorders. Small private or community hospitals sometimes offer neuropsychology services that serve a wide patient base from medical, to neurologic, to psychiatric conditions. In nursing homes, neuropsychologists are often asked to see residents to help with decisions about guardianship, capacity, and placement. In the private practice sector, neuropsychologists can be found in solo practices with single-provider clinics and specialty group practices that have a range of focus from neurology to behavioral health. Multidisciplinary private-practice clinics are often useful referral sources for complementary care (eg, neuropsychology, psychotherapy, and cognitive rehabilitation services all under 1 roof).

What Does the Neuropsychologist Do?

The neuropsychology visit is generally broken up into records review, an interview, testing, and feedback, which may be done in 1 or many days. The neuropsychologist reviews available records before seeing an individual for testing and returns to them during report writing. This process allows clarification of points during the interview, ensuring all data is taken into account when developing a differential diagnosis. Interviews range from a brief and targeted interview in someone who, for example, has already been seen by a neurologist in the same practice, to longer psychodiagnostic interviews for someone unknown to the neuropsychologist. The same day or soon after, the person being evaluated returns for testing, which may be administered by a neuropsychologist, psychometrician, or neuropsychology technician (state rules vary). Tests are then scored, and some neuropsychologists offer initial feedback the same day, whereas others offer feedback later or only through a written report. Reports are submitted to the medical record or referring provider. Depending on the setting, results may also be shared via rounds, other in-person meetings with referral sources, or in diagnostic case conferences.

What Is Neuropsychologic Testing?

Neuropsychologic tests use pencil-and-paper, question-and-answer, and computerized measures to assess cognition. These tests usually have standardized normative information available for comparison with healthy people in the same age range, often stratified by sex, education, and occasionally race. By performing a comprehensive battery of tests, usually with
several tests in each domain (Table), neuropsychologists establish a profile of strengths and weaknesses, which are considered the cognitive “phenotype,” and helps narrow the differential diagnosis.2 Multiple other pieces of information are integrated, including mood and behavior symptoms, medications, medical comorbidities, family history, medical history, and mitigating factors that may affect testing. These data, collected during the record review and interview, are taken into account in test data interpretation and contribute to the overall characterization of an individual’s neurobehavioral status.

### TABLE. NEUROPSYCHOLOGIC TESTS COMMONLY USED IN MEMORY DISORDER CLINICS BY DOMAIN

<table>
<thead>
<tr>
<th>Domain</th>
<th>Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premorbid intelligence</td>
<td>American National Adult Reading Test</td>
</tr>
<tr>
<td></td>
<td>Wide Range Achievement Test, 4th edition</td>
</tr>
<tr>
<td></td>
<td>Advanced Clinical Solutions Test of Premorbid Functioning</td>
</tr>
<tr>
<td>Memory-verbal memory</td>
<td>Rey Auditory Verbal Learning Test</td>
</tr>
<tr>
<td></td>
<td>California Verbal Learning Test—II</td>
</tr>
<tr>
<td></td>
<td>Hopkins Verbal Learning Test—Revised</td>
</tr>
<tr>
<td></td>
<td>WMS-IV Logical Memory</td>
</tr>
<tr>
<td>Memory-nonverbal memory</td>
<td>Rey-Osterreith Complex Figure Test</td>
</tr>
<tr>
<td></td>
<td>Brief Visuospatial Memory Test—Revised</td>
</tr>
<tr>
<td></td>
<td>WMS-IV Visual Reproduction</td>
</tr>
<tr>
<td>Attention</td>
<td>WAIS-IV Digit Span</td>
</tr>
<tr>
<td></td>
<td>WAIS-IV Digit Symbol Coding</td>
</tr>
<tr>
<td></td>
<td>WAIS-IV Symbol Search</td>
</tr>
<tr>
<td></td>
<td>Categorical or semantic fluency (eg, animals)</td>
</tr>
<tr>
<td></td>
<td>Phonemic fluency</td>
</tr>
<tr>
<td>Executive functions</td>
<td>Trail Making Test</td>
</tr>
<tr>
<td></td>
<td>Wisconsin Card Sorting Test</td>
</tr>
<tr>
<td></td>
<td>Stroop Test</td>
</tr>
<tr>
<td></td>
<td>WAIS-IV Matrix Reasoning</td>
</tr>
<tr>
<td>Language skills</td>
<td>Boston Naming Test</td>
</tr>
<tr>
<td></td>
<td>Western Aphasia Battery</td>
</tr>
<tr>
<td></td>
<td>Multilingual Aphasia Evaluation</td>
</tr>
<tr>
<td>Visuospatial skills</td>
<td>Judgment of Line Orientation</td>
</tr>
<tr>
<td></td>
<td>Hooper Visual Organization Test</td>
</tr>
<tr>
<td></td>
<td>WAIS-IV Block Design</td>
</tr>
</tbody>
</table>

This list is not a comprehensive but includes frequently used measures. Abbreviations: WAIS-IV, Wechsler Adult Intelligence Scale, 4th edition; WMS-IV, Wechsler Memory Scale, 4th edition.

### How Is Neuropsychologic Testing Interpreted?

The cognitive phenotype derived from a person’s performance and symptom presentation typically is mapped onto underlying neural networks based on our understanding of cognition in the brain and brain-behavior relationships. Cognitive manifestations of many diseases, including AD and other neurodegenerative disorders, tend to reflect underlying changes in particular networks that are selectively vulnerable to that disorder.3 This relationship allows neuropsychologists to identify whether a phenotype corresponds with these known vulnerabilities. Historical information such as time course and chronology of symptoms are incorporated to develop a full and detailed understanding of an individual’s condition. Similarly, demographic information (eg, sex, educational background, and medical history) are often important factors that may mitigate test performance.

### What Can Neuropsychologists Offer Neurologists?

Neuropsychologists have the gift of time not often afforded to neurologists during patient visits. The outpatient neuropsychologic examination lasts 2 to 8 hours, depending on clinician style, referral question, and ability of the person being evaluated to participate. By conducting a detailed clinical interview with the individual and their family (often with the opportunity to speak with family members separately) and combining that with information from comprehensive testing, the neuropsychologist can gather a depth of information difficult to achieve during routine neurology visits. Most neurologists are skilled at using well known screening measures (eg, the Mini-Mental State Examination [MMSE]4 and Montreal Cognitive Assessment [MoCA]).5 These screening tests do not give detailed information of symptom severity, specific patterns, or integration of how cognitive domains interact (eg, executive functioning deficits affecting memory performance). Neuropsychologists are specifically trained and have access to sensitive assessment tools designed to capture the presence of impairments relative to a normative sample.

Neuropsychologists offer neurologist colleagues a concise integrated summary of an individual’s neurocognitive status through a detailed written report. Information from the neuropsychologic evaluation can guide treatment options (eg, medication management), determine need for further diagnostic evaluation (eg, neuroimaging or biomarker testing), and provide support for the individual and their family (eg, referral to social work or supportive therapies). Depending on the referral question and state requirements, recommendations about guardianship, driving, continuing work, and capacity are often made. A collaborative relationship with a neuropsychologist contributes to a physician’s ability to provide a comprehensive high level of care, increasing diagnostic accuracy and fine-tuned treatment options and recommendations.
How Do Neuropsychologists Approach Alzheimer’s Disease and Associated Disorders?

Neuropsychologic measures differentiate between normal cognitive aging and impairment that extends beyond the typical aging process. Baseline neuropsychologic testing can determine whether an individual is experiencing normal age-related changes—informative for referring physician and the person referred, who receive education about normal aging in the context of their unique cognitive strengths and weaknesses. Evaluation of this population also provides an opportunity for neuropsychologists to support lifestyle factors that promote healthy aging (Case 1).

Case 1: Mr. Smith

Mr. Smith, age 68 was referred by his neurologist who cited memory complaints and a Montreal Cognitive Assessment score of 23 (30 possible), with points lost for delayed recall, clock drawing, and the trail making task. Results of Mr. Smith’s brain MRI showed mild atrophy in the parietal regions and intact hippocampal volumes. Mr. Smith and his wife reported ongoing forgetfulness for 2 to 3 years. He had some vascular risk factors, including hypercholesterolemia; was overweight and relied on junk food in his diet; but was otherwise healthy, although quite sedentary. He denied depression, anxiety, and other neuropsychiatric symptoms. His wife reported disrupted sleep with snoring and gasping for breath. They were referred previously for a sleep study, but he felt this would be a waste of time since it was “just sleep.” There was no known family history of dementia.

On testing, Mr. Smith had difficulty learning and recalling new information (shapes and words) and problems with sustaining attention or switching quickly between tasks. Naming, basic visuospatial function, and most aspects of executive function were intact. His wife reported minimal change in his daily functioning, and he reported some daytime sleepiness on questionnaires.

At feedback, his apparent memory difficulties and risk of Alzheimer’s disease for his age group were explained. Feedback focused on modifiable risk factors, especially sleep, diet, and exercise. The family decided to follow the advice and return for reassessment.

A year later, Mr. Smith reported feeling much better. Although his lifestyle choices had not changed dramatically, he had been diagnosed with sleep apnea and began using continuous positive airway pressure (CPAP), which he tolerated well. On testing, some slowness and inefficient recall remained, but all scores were broadly within normal limits.

Although this type of dramatic turnaround is not common, it does happen. By leveraging the neuropsychologist’s ability to spend time with a person during interview and feedback and provide explanation and education, a reversible mimic of dementia was identified and successfully treated.

In some cases, cognitive changes are exaggerated with respect to normal aging, although the changes do not significantly affect an individual’s ability to function independently. Mild cognitive impairment (MCI) describes this level of dysfunction and may sometimes be a prodrome to future decline and dementia. Depending on cognitive phenotype and other factors, a neuropsychologist may consider this due to AD or another neurodegenerative disease. Many people with MCI will not progress to have AD or other neurodegenerative diseases, however. Early detection of cognitive changes in persons with MCI is important for assisting the individual and their medical team with suggestions of modifiable lifestyle factors such as diet and exercise, known to contribute to brain health.

If a person is identified as having impairments beyond what is expected for their age, and these impairments interfere with functional ability with indications of insidious decline over time, a diagnosis of dementia may be given. The cognitive phenotype guides the clinician to make inferences about underlying changes in specific neural networks or determining whether other concerning conditions are at play (eg, a primary psychiatric condition like depression, sleep apnea, or risk from prior concussion history). For example, the pattern of cognitive impairment across domains can assist with elucidating concerns for a neurodegenerative disease such as vascular cognitive impairment (VCI) or dementia with Lewy bodies (DLB), or an atypical dementia such as frontotemporal degeneration (Case 2). Neuropsychologists can assist in other ways; for example, a presurgical neuropsychologic evaluation can determine whether dementia is present in a person with Parkinson’s disease who is a candidate for deep brain stimulation.

With respect to AD, which typically initially presents as a primary memory disorder, neuropsychologists are able to select from a variety of verbal and nonverbal memory assessment tools sensitive to memory impairment that examine ability to:
1. learn new information with repeated exposure,
2. spontaneously retrieve previously learned material after short and long delays, and
3. discriminate and choose target information from related distracting information.

Such assessment gives a clinician the ability to hypothesize a disruption to neural networks of memory function and, when integrated with performance in other domains, to determine primary areas of impairment. Neurodegenerative syndromes are differentiated through use of the clinical profile, symptom history, and symptom chronology. Establishing a baseline level of cognitive functioning allows for tracking an individual over time to assess change. An annual monitoring process can assist with diagnostic clarity, treatment planning, and education and support for individuals and their families (Case 3).

Neuropsychologic assessment improves precision of diagnosis and prognosis for individuals seen in memory clinics, and memory measures alone have comparable or better sensitivity...
and specificity than many biomarkers. Combining imaging or cerebrospinal fluid (CSF) biomarkers with neuropsychology will likely increase accuracy of diagnostic classification.

Neuropsychology and Technology

Technology offers many exciting opportunities for neuropsychology. Testing with computer-based methods can lessen subjectivity and human error and cost less to the consumer. Many people carry smartphones or smart watches that can help collect data more continuously, removing the need for clinicians to rely on a single time-point or in-office testing. These new opportunities have led to development of tablet-based cognitive testing, which, it is suggested, may be administered in the absence of a psychometrician at least for unimpaired or minimally impaired adults, mean age approximately 71.5. Burst cognitive testing on smartphones or tablets prompts a person to complete multiple brief cognitive tests several times a day over consecutive days. These tests are still being

CASE 2. Mr. Elbert

Mr. Elbert, age 55, was referred for problems with memory and word-finding difficulty that has worsened over the last 1 to 2 years. He reports problems "remembering words when speaking", an inability to think of the names of common objects, problems with reading and spelling, and difficulty following fast conversations. These problems interfered with his ability to give presentations at work and to be effective when communicating with his clients. His wife was very concerned about these changes that were noticeable in their everyday interactions together.

Mr. Elbert denied problems with other daily functioning including driving, paying bills, and managing his schedule. He described his sleep as "excellent," and although he reported no symptoms of depression or anxiety, he expressed concern and worry about himself and his future, stating that his communication challenges have made him more withdrawn.

Mr. Elbert’s performance on neuropsychologic tests revealed primary dysfunction in the language domain, including severely impaired object naming and moderately impaired verbal fluency. He had mild impairments in spelling and sentence comprehension. Although his spontaneous speech was intact, he often used nonspecific and general words in conversation and seemed to have difficulty with specific word choice. His verbal learning and delayed memory were severely impaired in the context of mildly suppressed nonverbal memory skills. Visual-spatial skills, executive functions, attention, and processing speed were relatively intact.

Mr. Elbert’s neuropsychologic profile raises concern for frontotemporal dementia (FTD). Given the insidious and preferential decline of language skills relative to other cognitive domains, he was felt to be experiencing the primary progressive aphasia variant of FTD.

Mr. Elbert was referred to a speech-language pathologist for support with language deficits. He and his family were referred to a social worker for education, support, and care planning services. He was advised to return for annual follow-up to further track and monitor his cognitive skills.

CASE 3. Mrs. Jones

Mrs. Jones, age 75, was referred for concern about memory decline. She denies problems with her memory stating defensively, "My life is routine…nothing much changes." Her husband and children describe a 2-year history of increasingly noticeable changes in her memory and behavior including forgetfulness in conversation, misplacing personal items, and requiring reminders for everyday tasks. Behaviorally, she demonstrated decreased interest in her hobbies and no longer called her sister for their daily phone chats. Her family expresses discomfort when she drives, because she seems uncertain, distracted, and easily disoriented in unfamiliar surroundings. She sleeps well and denies feeling depressed or anxious. There were no reported problems with independent personal tasks such as bathing, dressing, or eating, and she prepares simple meals without difficulty.

Neuropsychologic testing reveals problems learning new information with repeated exposure, and an inability to recall any information after a brief period of time. Mrs. Jones’ test performance reveals additional impairments in the areas of semantic verbal fluency and object naming, as well as verbal reasoning skills and divided attention. She has relatively preserved performance in visual-spatial abilities and basic attentional capacity. Mrs. Jones’ neurocognitive profile therefore reveals primary and severe impairment in memory functions, mild executive dysfunction and suppression on language tasks. These insidious and progressively worsening changes caused a mild degree of functional impairment that was not otherwise accounted for by medical causes, sleep disturbance, or mood disorder.

Mrs. Jones’ cognitive phenotype was most reflective of an underlying degenerative process implicating limbic dysfunction and a clinical diagnosis of probable Alzheimer’s disease.

Mrs. Jones and her family were given supportive education about dementia and memory disorder, recommendations for care planning, and encouragement to consider cognitive rehabilitation with a speech-language pathologist skilled at working with people who have dementia. The family was advised to return annually for repeat testing to track and monitor Mrs. Jones’ abilities and to further assist with treatment planning.
Neuropsychological Testing in the Age of Biomarkers

The most recent proposed research diagnostic guidelines do not require cognitive impairment to diagnose earliest stages of AD. The guidelines rely on amyloid, tau and neurodegeneration status from imaging studies to provide diagnoses of preclinical and prodromal AD and are controversial. A large percentage of people found to have a positive amyloid status via CSF or positron emission tomography (PET) scan will never develop dementia. Because of resilience and cognitive reserve, among other factors, there is large variation in when dementia will emerge in individuals with positive biomarker findings. Cognitive testing is important even when there is biomarker positivity to determine the actual presence of decline and provide prognostic value and appropriate recommendations.


Jennifer Medina, PhD
Clinical Neuropsychologist
CEO & Founder
Rocky Mountain Neurobehavioral Associates
Denver, CO

Sarah J. Banks PhD ABPP-CN
Associate Professor
Departments of Neurology and Psychiatry
University of California, San Diego
San Diego, CA

Disclosures
JM has disclosures at www.practicalneurology.com.