Cognitive Complaints and Neuropsychologic Testing

When should neuropsychologic tests be ordered and what questions should testing answer?

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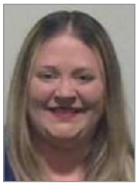


What Can Be Learned?

Neuropsychologic testing involves an extensive, standardized evaluation for and quantification of cognitive deficits across multiple domains, including orientation, processing speed, attention and concentration, language, verbal and visual memory, calculation, constructional praxis, executive function, higher-order reasoning, psychiatric symptoms, and level of effort during testing. Each cognitive domain can be localized to a functional neuroanatomic or neural network correlate that implicates specific brain regions. For example, processing speed relies upon intact deep frontal white matter tracts. Expressive language localizes to Broca's area and receptive language to Wernicke's. Verbal memory can be considered more left hemispheric, whereas visual memory is primarily on the right. Poor calculation with finger agnosia, left/right confusion, and agraphia represents Gerstmann's syndrome, which localizes to the supramarginal left parietal gyrus, an area affected early in Alzheimer's disease (AD) dementia. Executive function is a dorsolateral prefrontal task. Constructional praxis and higher-order reasoning involve multimodal brain regions.

Initial testing provides a relative baseline, helps differentiate causes of cognitive impairment and neurodegenerative conditions, and assesses competencies (eg, driving, financial decision making, need for increased supervision). In patients with dementia or cognitive impairment caused by another neurologic condition (eg, traumatic brain injury, multiple sclerosis, epilepsy), repeat testing provides objective data regarding disease course and response to treatment vis-à-vis cognition. For primary cognitive disorders, neuropsychologic testing allows more accurate differentiation of normal aging, subtypes of mild cognitive impairment (MCI), and dementia. Accurate assessment guides treatment decisions, counseling about prognosis and expected course of illness, and the appropriate level of supportive care required for safety.

When and How to Order

Patients who screen positive for impairment on a brief cognitive assessment (ie, Folstein Mini-Mental State Examination or Montreal Cognitive Assessment) should be referred for formal neuropsychologic testing.[1] Early referrals for those at risk of cognitive decline from many sources (eg, suspected neurodegenerative conditions, epilepsy, multiple sclerosis, and neuropsychiatric conditions) help to provide a more robust baseline for later comparison as neurologic diseases progress.

To maximize the usefulness of neuropsychologic testing, the referral questions should be as specific as possible regarding the clinical questions in play. For example, many referrals consist of as little as saying, "differential diagnosis." It is often more fruitful to specify instead whether there is concern for multiple etiologies, a need for clarification on level of progression, questions about the effects on insight or judgment, or any other specific factors that can influence cognitive function (eg, psychiatric conditions). Multiple specific questions can be addressed in the referral, but the more specific the question is, the more directly the neuropsychologist can tailor the assessment to provide useful information.

Neuropsychologists vary in taking a more fixed or flexible battery approach. Those who use a fixed battery of tests give nearly all patients the same tests. Those who use a flexible battery select tests for each patient individually. Another approach is a fixed–flexible battery that administers a relatively fixed battery to assess the most common domains in question but adds measures based on specific referral question and the individual. Clearly specifying referral questions can lead to adjustments in the battery of tests performed to provide more accurate answers.

Establishing a Baseline

As dementia implies a decline from a lifelong cognitive baseline, it is important that the neuropsychologic assessment include an estimation of premorbid mental ability. This can be estimated in multiple ways (Box 1).[2]

It is generally recommended that a collateral source accompany patients to their neuropsychologic evaluation, if possible. When collateral information is not available and the patient is not a reliable historian, or to supplement history given by the patient and a collateral informant, it is common to estimate premorbid levels of intelligence by measuring more crystallized forms of knowledge, such as irregular word-reading tests that are believed to be relatively resistant to change with cognitive aging. These tests are generally robust estimates of premorbid intelligence and often the most highly correlated with full-scale IQ scores over time. Examples include the Wechsler Test of Adult Reading (WTAR), Wide Range Achievement Test reading subscale (WRAT), North American Adult Reading Test (NAART), or National Adult Reading Test (NART). These tests all involve pronunciation of 50 or so irregular English words; the more words read correctly, the higher the estimate of premorbid functioning. In a case–control study, after controlling for age 11 IQ, mean NART scores did not differ in people with and without dementia (average age 80).[3] However, in a larger longitudinal study with the WTAR, there was a slight decline (3.01) of words read correctly in patients with MCI and a more severe decline (7.39) in patients with AD. Thus, such tests may underestimate premorbid IQ compared to demographic-based predictions.[2]

Diagnosis

Memory Deficits, Mild Cognitive Impairment, and Dementia

Deficits in immediate and delayed memory during testing are sensitive and specific for MCI and AD.[4] Variances within neuropsychologic profiles of people with MCI predict the likelihood of progression to AD. Both single-domain amnestic and multiple-domain amnestic types have a relatively higher risk of progressing to AD than either single-domain nonamnestic or multiple-domain nonamnestic subtypes.[5] The more severe the deficits, the greater the risk for dementia, which may inform frequency of follow-up and patient/family education regarding prognosis and treatment. Patients who meet criteria for MCI should be reassessed in 1 year to evaluate for further decline,[6] as AD can be identified at an earlier stage by focusing on intraindividual change rather than comparison to group norms.[7] In contrast, improved performance after 1 year argues against a neurodegenerative process.

When evaluating for a formal dementia diagnosis, neuropsychologic instruments that emphasize memory function are the most useful. For example, 5 subtest of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) Neuropsychological Battery—animal naming, Modified Boston Naming Test, Mini-Mental State Examination, constructional praxis, and word list memory—are reliable measures of cognition in normal aging versus in patients with AD.[8]

Neuropsychologic testing can also identify deficit clusters suggestive of specific etiologies in conjunction with history, mental status, neurologic examinations, neuroimaging, and cerebrospinal fluid analysis. Patients with vascular dementia (VaD) have superior verbal long-term memory and inferior frontal executive function compared with patients with AD.[9] Executive dysfunction correlates with severity of subcortical lesion load and typically presents prior to severe memory loss.[10] As with evaluation for MCI progression to AD, repeat assessment will assist in evaluating static vs progressive changes (eg, poststroke vs a progressive neurodegenerative syndrome) and help in assessing competencies such as driving, financial decision making, and any need for increased supervision. Patients with frontotemporal lobar degeneration (FTLD) have higher scores than patients with AD on tests of orientation, memory, and general cognitive ability. Patients with AD score better than patients with FTLD on verbal ability, although there is considerable overlap.[11] Patients with dementia with Lewy bodies (DLB) have lower scores than patients with AD on measures of visuospatial function and higher scores on measures of memory and language function.[12]

Psychiatric Diagnoses

Neuropsychologic testing may also help delineate if depression or other psychiatric symptoms (eg, executive dysfunction in schizophrenia) are contributing or causative factors for subjective cognitive decline, which is otherwise an early indicator for development of MCI. However, because many psychiatric symptoms co-occur with neurocognitive disorders and may even be the first sign of a neurocognitive disorder,[13] parsing this out can be difficult. Clinically, when there are questions regarding whether neuropsychologic

Box 1. Methods to Estimate Premorbid Baseline Functioning

Demographic-based predictions such as educational or occupational attainment.

Estimates of adult functioning abilities (managing home, work, finances) based on patient's history including data from a collateral informant.

Learned knowledge that is relatively resistant to changes seen in cognitive aging, such as irregular word reading.[2]

Box 2. Sample Referral Questions to Asses Comorbid vs Symptomatic Issues

"Is this typical aging with schizophrenia/depression or does this also include indications of neurodegeneration beyond what would be expected?"

"Are the patient's hallucinations typical of dementia with Lewy bodies, or does this include indications of psychiatric disease beyond what would be expected?"

"Are the depressive symptoms typical of a patient with a chronic illness, such as MS, or may there be an underlying mood disorder?"

deficits may be comorbid vs symptomatic, it is helpful to specify that in the referral (Box 2).

Psychiatric symptoms such as late-onset depression can also be prodromal to the onset of dementia[7] and may be an indication for neuropsychologic assessment. Onset of decline within the last 5 years, age at onset above 60 years, and associated concerns about decline confirmed by an informant are suggestive of a neurodegenerative disorder.[14] Apathy, irritability, and abnormal nighttime behaviors may be associated factors.[15]

Limitations

Although neuropsychologic testing can be informative, it has some limitations. Testing may be influenced by primary language, educational level, and age.[16] Neuropsychologists need to keep updated on new and more specific normative reference groups to tailor interpretation to the individual patient and best answer referral questions. Poor effort during testing may invalidate results and make accurate interpretation difficult. Neuropsychologists generally include effort measures and interpret the results in the context of the level of effort the patient exhibited during testing.

As is the case with other ancillary tests, neuropsychologic testing cannot make or break a diagnosis of dementia. However, in combination with patient history, examination, and other possible ancillary tests (structural and functional neuroimaging, CSF protein markers), neuropsychologic testing can improve diagnostic accuracy. It provides noninvasive, measurable, and trackable data points to evaluate treatment efficacy and individual disease course and aids in counseling regarding prognosis and appropriate level of independence in patients with cognitive impairment.

Summary

Neuropsychologic reports are most beneficial when the referral questions are as specific and comprehensive as possible, and the neuropsychologist has taken steps to clearly define any present limitations to testing and interpret the results in an individualized manner. ■

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