We have all treated a patient for whom you know you had the diagnosis correct, the medication regimen was working, and the patient adhered to treatment, but something was still “off.” There was something cognitively that wasn’t right, and you had identified subtle (and some overt) errors in the standard psychiatric cognitive assessment that didn’t seem amenable to psychotropic medications. Perhaps what was needed was neuropsychological testing, one of the most useful but underutilized resources available to help fine-tune diagnosis and treatment. Finding a neuropsychologist who is sensitive to the unique needs of patients with psychiatric disorders, and knowing what and how to communicate the clinical picture and need for the referral, can be challenging due to the limited availability, time, and cost of a full battery of standardized tests.

This article describes the purpose of neuropsychological testing, why it is an important part of psychiatry, and how to make the best use of it.

**What is neuropsychological testing?**

Neuropsychological testing is a comprehensive evaluation designed to assess cognitive functioning, such as attention, language, learning, memory, and visuospatial and executive functioning. Neuropsychology has its own vocabulary and lexicon that are important for psychiatric clinicians to understand. Some terms, such as aphasia, working memory, and dementia, are familiar to many clinicians. However, others, such as...
information processing speed, performance validity testing, and semantic memory, might not be. Common neuropsychological terms are defined in Table 1 (page 42).

The neuropsychologist’s role
A neuropsychologist is a psychologist with advanced training in brain-behavior relationships who can help determine if cognitive problems are related to neurologic, medical, or psychiatric factors. A neuropsychological evaluation can identify the etiology of a patient’s cognitive difficulties, such as stroke, poorly controlled diabetes, or mental health symptoms, to help guide treatment. It can be difficult to determine if a patient who is experiencing significant cognitive, functional, or behavioral changes has an underlying cognitive disorder (e.g., dementia or major neurocognitive disorder) or something else, such as a psychiatric condition. Indeed, many psychiatric conditions, including schizophrenia, bipolar disorder, posttraumatic stress disorder (PTSD), and major depressive disorder (MDD), can present with significant cognitive difficulties. Thus, when patients report an increase in forgetfulness or changes in their ability to care for themselves, neuropsychological testing can help determine the cause.

How to refer to a neuropsychologist
Developing a referral network with a neuropsychologist should be a component of establishing a psychiatric practice. A neuropsychologist can help identify deficits that may interfere with the patient’s ability to adhere to a treatment plan, monitor medications, or actively participate in treatment and therapy. When making a referral for neuropsychological testing, it is important to be clear about the specific concerns so the neuropsychologist knows how to best evaluate the patient. A psychiatric clinician does not order specific neuropsychological tests, but thoroughly describes the problem so the neuropsychologist can determine the appropriate tests after interviewing the patient. For example, if a patient reports memory problems, it is essential to give the neuropsychologist specific clinical data so he/she can determine if the symptoms are due to a neurodegenerative or psychiatric condition. Then, after interviewing the patient (and, possibly, a family member), the neuropsychologist can construct a battery of tests to best answer the question.

Which neuropsychological tests are available?
There is a large battery of neuropsychological tests that require a licensed psychologist to administer and interpret. Those commonly used in research and practice to differentiate neurologically-based cognitive deficits associated with psychiatric disorders include the Wechsler Adult Intelligence Scale-4th edition (WAIS-IV) for assessing intelligence, the California Verbal Learning Test-Third Edition (CVLT-3) for verbal memory and learning, the Brief Visuospatial Memory Test-Revised for visual memory, the Wisconsin Card Sorting Test (WCST) for executive functions, and the Ruff 2&7 Selective Attention Test for sustained attention. These and other commonly used tests are described in Table 2 (page 43).1

Neuropsychological testing vs psychological testing
The neuropsychologist will use psychometric properties (such as the validity and reliability of the test) and available normative data to pick the most appropriate tests. To date, there are no specific tests that clearly delineate psychiatric from nonpsychiatric etiologies, although the Screen for Cognitive Impairment in Psychiatry (SCIP) was developed in 2013 to explore cognitive abilities in the functional psychoses; it is beginning to be used in other studies.5 The neuropsychologist will consider the patient’s current concerns, the onset and progression of these concerns, and the pattern in testing behavior to help determine if psychiatric conditions are the most likely etiology.

In addition to cognitive tests, the neuropsychologist might also administer psychological tests. These might include commonly used screening tools such as the
Neuropsychological testing

Patient Health Questionnaire-9 (PHQ-9)\textsuperscript{6} or Geriatric Depression Scale (GDS),\textsuperscript{7} or more comprehensive objective personality measures, such as the Minnesota Multiphasic Personality Inventory-2-Restructured Format (MMPI-2-RF),\textsuperscript{8} or Personality Assessment Inventory (PAI).\textsuperscript{9} These tests, along with a thorough clinical history, can help identify if a psychiatric condition is present. In addition, for the more extensive tests such as the MMPI-2-RF or PAI, there are certain neuropsychological profiles that are consistent with a psychiatric etiology for cognitive difficulties. These profiles are formulated based on specific test scores in combination with complex patient variables.

**Understanding the report**

While there will be stylistic differences in reports depending on the neuropsychologist’s setting, referral source, and personal preferences, most will include discussion of why the patient was referred for evaluation and a description of the onset and progression of the problem.\textsuperscript{10} Reports often also include pertinent medical and psychiatric history, substance use history, and family
Issues of validity are monitored to determine if the results are consistent with known neurologic patterns.

Why is neuropsychological testing important?
Schizophrenia, MDD, bipolar disorder, and PTSD produce significant neurobiologic changes that often result in deterioration of a patient’s global cognitive function. Increased emphasis and attention in psychiatric research have yielded more clues to the neurobiology of cognition. However, even though many psychiatric clinicians are trained in cognitive assessments, such as the “clock test,” “serial sevens,” “numbers forward and backward,” “proverb,” and “word recall,” and common scenarios to evaluate judgment and insight, such as “mailing a letter” and “smoke in a movie theatre,” most of these components are not completed during a standard psychiatric evaluation. Because the time allotted to completing a psychiatric evaluation

<table>
<thead>
<tr>
<th>Test</th>
<th>Functions and subdomains explored</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wechsler Adult Intelligence Scale-4th Edition (WAIS-IV)</td>
<td>IQ including verbal, perceptual processes, working memory, and processing speed scales</td>
</tr>
<tr>
<td>Wechsler Memory Scale-4th Edition (WMS-IV)</td>
<td>Measures multiple aspects of memory</td>
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<tr>
<td>Rey Complex Figure Test (RCFT)</td>
<td>Construction and visuospatial memory</td>
</tr>
<tr>
<td>Trail Making Test</td>
<td>Visual search speed, scanning, and switching</td>
</tr>
<tr>
<td>Symbol Digit Modalities Test (SDMT)</td>
<td>Visual scanning, tracking, and speed of processing</td>
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<tr>
<td>Stroop test</td>
<td>Inhibitory control and selective attention</td>
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<tr>
<td>Verbal Fluency test</td>
<td>Ability to quickly access words</td>
</tr>
<tr>
<td>Wisconsin Card-Sorting Test (WCST)</td>
<td>Reasoning, cognitive flexibility, and abstraction</td>
</tr>
<tr>
<td>Clock-drawing test</td>
<td>Visuospatial and praxis abilities</td>
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<tr>
<td>Token Test (TT)</td>
<td>Verbal comprehens</td>
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Neuropsychological testing continues to be shortened, it is sometimes difficult to complete the “6 bullets” required by the Centers for Medicare & Medicaid Services as part of the mental status exam (Table 3). To date, the best evidence for neuropsychological deficits exists for patients with schizophrenia, bipolar disorder, MDD, and PTSD. The Box (page 45) describes the findings of studies of neuropsychological deficits in patients with schizophrenia and bipolar disorder.

Neuropsychological testing: 2 Case studies

The following 2 cases illustrate the pivotal role of neuropsychological testing in formulating an accurate differential diagnosis, and facilitating improved outcomes.

CASE 1
A veteran with PTSD and memory complaints

Mr. J, age 70, is a married man who spent his career in the military, including combat service in the Vietnam War. His service in Vietnam included an event in which he couldn’t save platoon members from an ambush and death in a firefight, after which he developed PTSD. He retired after 25 years of service.

Mr. J’s psychiatrist refers him to a neuropsychologist for complaints of memory difficulties, including a fear that he’s developing Alzheimer’s disease (AD). Because of the concern for AD, he undergoes tests of learning and memory, such as the CVLT-3, the Brief Visuospatial Memory Test-Revised, and the Logical Memory subtest from the Wechsler Memory Scale–4th Edition. Other tests include a measure of confrontation naming, verbal fluency (phonemic and semantic fluency), construction, attention, processing speed, and problem solving. In addition, a measure of psychiatric and emotional functioning is also administered (the MMPI-2-RF).

The results determined that Mr. J’s subjective experience of recall deficits is better explained by anxiety resulting from the cumulative impact of day-to-day emotional stress in the setting of chronic PTSD. Mr. J was experiencing cognitive sequelae from a complicated emotional dynamic, comprised of situational stress, amplified by coping difficulties that were rooted in older post-traumatic symptoms. These emotions, and the cognitive load they generated, interfered with the normal processes of attention and organization necessary for the encoding of information to be remembered. He described being visibly angered by the clutter in his home (the result of multiple people living there, including a young grandchild), having his efforts to get things done interrupted by the needs of others, and a perceived loss of control gradually generalized to even mundane circumstances, as often occurs with traumatic responses. In short, he was chronically overwhelmed and not experiencing the beginnings of dementia.

For Mr. J, neuropsychological testing helped define the focus and course of therapy. If he had been diagnosed with a major neurocognitive disorder, therapy might have taken a more acceptance and grief-based approach, to help him adjust to a chronic, potentially life-limiting condition. Because this diagnosis was ruled out, and his cognitive complaints were determined to be secondary to a core diagnosis of PTSD, therapy instead focused on treating PTSD.

CASE 2
A 55-year-old with bipolar I disorder

Mr. S, age 55, is taken to the emergency department (ED) because of his complaints of a severe headache. While undergoing brain MRI, Mr. S becomes highly agitated
Neuropsychological testing and functionality in schizophrenia and bipolar disorder

Patients with schizophrenia have been the subjects of neuropsychological testing for decades. The results have shown deficits on many standardized tests, including those of attention, memory, and executive functioning, although some patients might perform within normal limits.15

A federal initiative through the National Institute of Mental Health (NIMH) known as MATRICS (Measurement and Treatment Research to Improve Cognition in Schizophrenia) was developed in the late 1990s to develop consensus on the underlying cognitive deficits in schizophrenia. MATRICS was created with the hopes that it would allow the FDA to approve treatments for those cognitive deficits independent of psychosis because current psychotropic medications have minimal efficacy on cognition.16,17 The MATRICS group identified working memory, attention/vigilance, verbal learning and memory, visual learning and memory, speed of processing, reasoning and problem solving, and social cognition as the key cognitive domains most affected in schizophrenia.14 The initial program has since evolved into 3 distinct NIMH programs: CNTRICS16 (Cognitive Neuroscience Treatment Research to Improve Cognition in Schizophrenia), TURNS19 (Treatment Units for Research on Neurocognition in Schizophrenia), and TENETS20 (Treatment and Evaluation Network for Trials in Schizophrenia). The combination of neuropsychological testing and neuroimaging has led to the conceptualization of schizophrenia as a neurodevelopmental disorder.

Individuals at risk for psychosis
As clinicians, we have long heard from parents of children with schizophrenia a standard trajectory of functional decline: early premorbid changes, a fairly measurable prodromal period marked by subtle deterioration in cognitive functioning, followed by the actual illness trajectory. In a recent meta-analysis, researchers compared the results of 60 neuropsychological tests comprising 9 domains in people who were at clinical high risk for psychosis who eventually converted to a psychotic disorder (CHR-P), those at clinical high risk who did not convert to psychosis (CHR-NP), and healthy controls.21 They found that neuropsychological performance deficits were greater in CHR-P individuals than in those in the CHR-NP group, and both had greater deficits than healthy controls.

For many patients with schizophrenia, full cognitive maturation is never reached.22 In general, decreased motivation in schizophrenia has been correlated with neurocognitive deficits.23

Schizophrenia vs bipolar disorder
In a study comparing neuropsychological functioning in patients with schizophrenia and bipolar disorder with psychotic features (BP-P), researchers found greater deficits in schizophrenia, including immediate verbal recall, working memory, processing speed, and verbal fluency.22 Patients with BP-P demonstrated impairment consistent with generalized impairment in verbal learning and memory, working memory, and processing speed.22

Children/adolescents
In a recent study comparing child and adolescent offspring of patients with schizophrenia (n = 41) and bipolar disorder (n = 90), researchers identified neuropsychological deficits in visual memory for both groups, suggesting common genetic linkages. The schizophrenia offspring demonstrated impairment consistent with generalized impairment in verbal learning and memory, working memory, and processing speed.22

Information processing
Another study compared the results of neuropsychological testing and the P300 component of auditory event-related potential (an electrophysiological measure) in 30 patients with schizophrenia, siblings without illness, and normal controls.24 The battery of neuropsychological tests included the Digit Symbol Substitution Test, Digit Vigilance Test, Trail Making Test-B, and Stroop test. The P300 is well correlated with information processing. Researchers found decreased P300 amplitude and latency in the patients and normal levels in the controls; siblings scored somewhere in between.24 Scores on the neuropsychological tests were consistently below normal in both patients and their siblings, with patients scoring the lowest.24

and aggressive to the radiology staff and is transferred to the psychiatric inpatient unit. He has a history of bipolar disorder that was treated with lithium approximately 20 years ago. Due to continued agitation, he is transferred to the state hospital and prescribed multiple medications, including an unspecified first-generation antipsychotic (FGA) that results in drooling and causes him to stoop and shuffle.

Mr. S’s wife contacts a community psychiatrist after becoming frustrated by her inability to communicate with the staff at the state hospital. During a 1-hour consult, she reveals that Mr. S was a competitive speedboat racer and had suffered numerous concussions due
to accidents; at least 3 of these concussions that occurred when he was in his 20s and 30s had included a loss of consciousness. Mr. S had always been treated in the ED, and never required hospitalization. He had a previous marriage, was estranged from his ex-wife and 3 children, and has a history of alcohol abuse.

The MRI taken in the ED reveals numerous patches of scar tissue throughout the cortex, most notably in the striatum areas. The psychiatrist suspects that Mr. S’s agitation and irritation were related to focal seizure activity. He encourages Mr. S’s wife to speak with the attending psychiatrist at the state hospital and ask for him to be discharged home under her care.

Eventually, Mr. S is referred for a neurologic consult and neuropsychological testing. The testing included measures of attention and working, learning and memory, and executive functioning. The results reveal numerous deficits that Mr. S had been able to compensate for when he was younger, including problems with recall of newly learned information and difficulty modifying his behavior according to feedback. Mr. S is weaned from high doses of the FGA and is stabilized on 2 antiepileptic agents, sertraline, and low-dose olanzapine. A rehabilitation plan is developed, and Mr. S remains out of the hospital.

A team-based approach
Psychiatric clinicians need to recognize the subtle as well as overt cognitive deficits present in patients with many of the illnesses that we treat on a daily basis. In this era of performance- and value-based care, it is important to understand the common neuropsychological tests available to assist in providing patient-centered care tailored to specific cognitive deficits. Including a neuropsychologist is essential to implementing a team-based approach.

Clinical Point
Psychiatric clinicians need to recognize the subtle as well as overt cognitive deficits present in the patients we treat on a daily basis.

Related Resources

Drug Brand Names
Lithium - Eskalith, Lithobid
Olanzapine - Zyprexa
Sertraline - Zoloft

Bottom Line
Neuropsychological testing can help pinpoint key cognitive deficits that interfere with the potential for optimal patient outcomes. Psychiatric clinicians need to be knowledgeable about the common tests used and how to incorporate the results into their diagnosis and treatment plans.

References

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