The Neuropsychiatric Approach to the Assessment of Patients in Neurology

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Abstract

Neuropsychiatry is a clinical neuroscience specialty focused on the evaluation and treatment of patients who present with symptoms at the intersection of neurology and psychiatry. Neuropsychiatrists assess and manage the cognitive, affective, behavioral, and perceptual manifestations of disorders of the central nervous system. Although fellowship training in behavioral neurology-neuropsychiatry exists in the United States and several other countries internationally, the need for neuropsychiatric expertise greatly outweighs the number of specialists in practice or training. This article serves as a primer for both neurologists and psychiatrists seeking to improve or refresh their knowledge of the neuropsychiatric assessment, including detailing aspects of the history-taking, physical exam, psychometric testing, and associated diagnostic work-up. In doing so, we urge the next generation of neurologists and psychiatrists to take on both the opportunity and challenge to work at the intersection of both clinical neuroscience specialties using an integrated neuropsychiatric perspective.

Keywords
- neuropsychiatry
- assessment
- behavioral neurology
- interview
- education

The assessment and management of patients in neurology manifesting cognitive, affective, behavioral, and/or perceptual symptoms can be some of the most complex and potentially daunting tasks for neurologists and psychiatrists alike.[1] There are many reasons for this—the complex nature of the symptoms, the lack of easily deployable and objective measures to characterize symptoms or establish diagnosis, the sometimes laborious and extensive disease history involved (with at times an affectively-laden storyteller), and the unfortunate stigma surrounding mental health symptoms in general. This is further complicated by the fact that neurologists and psychiatrists spend only a small minority of their time training in the complementary specialty during their residency.[2,3] The fellowship training programs in behavioral neurology (BN) and neuropsychiatry (NP) are borne out of this identified need for subspecialty training at the intersection of neurology and psychiatry. These two subspecialties have fused over the years (termed "BNNP") in the United States, now adopting common fellowship training objectives, board examination content, and credentialing via the United Council for Neurologic Subspecialties (UCNS), accessible from both psychiatry and neurology residency training programs.[4,5] The UCNS website currently identifies 42 U.S. programs in BNNP. This article is designed to outline the approach to assessing and evaluating the patient with prominent neuropsychiatric symptoms, and to provide a primer for neurologists and psychiatrists seeking additional guidance as well as a practical framework for such encounters. Additionally, a related overarching goal is to energize the next generation of neurologists and

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psychiatrists to develop an element of shared, partially overlapping expertise in at least a subset of clinical neuroscience providers.[5]

NP is a clinical neuroscience specialty that serves to evaluate and manage patients who present with symptoms at the intersection of neurology and psychiatry. Neuropsychiatrists manage the traditionally-conceptualized "psychiatric" manifestations of disorders of the central nervous system—these are often interpreted as disorders manifesting behavioral, emotional, cognitive and/or perceptual dysfunction in addition to the sensorimotor and language abnormalities of other neurological disorders. The field has evolved over time with the growing and changing knowledge of clinical neuroscience. For example, the domain of psychiatrists previously included managing patients with epilepsy, encephalitis, and neurological manifestations of syphilis, before the etiologies and focused treatments for these conditions were more clearly understood.[6–8] As emerging technology enables deeper understanding of many neurological and psychiatric conditions, it has become increasingly evident that many neurological conditions have behavioral and affective manifestations, and vice versa. The dichotomy grows increasingly arbitrary as new information surfaces, leading many to propose a re-integration of the fields of neurology and psychiatry based on the notion that all mental disorders reside in the brain, and all neuropsychiatric disorders would benefit from a biopsychosocial formulation and treatment plan. This BNNP integration may lead to better care for patients as clinicians develop training and understanding in the diagnosis and treatment of a wider range of conditions affecting various aspects of neurological functioning; prototypical diagnoses for a BNNP clinician include Parkinson's disease psychosis, Alzheimer's disease with behavioral disturbance, psychiatric sequelae of traumatic brain injury, psychiatric comorbidities of epilepsy, and functional neurological disorder among other conditions.

Taking a Neuropsychiatric History—General Concepts

The components of the neuropsychiatric history are similar to those obtained in other areas of medicine, but often with extra emphasis on a patient's experience of an event, careful screening for underlying or comorbid psychiatric and neurological conditions, and a more detailed social and developmental history. This approach follows a biopsychosocial framework, acknowledging the clinical importance of biological, psychological, and social factors on a patient's experience of disease or illness. Many of the diagnoses in NP hinge on historical details of a case or the subjective report of a patient or collateral informant were supported or augmented by specific laboratory findings, neuroimaging data, neuropsychological testing abnormalities, or the lack thereof. A list of neuropsychiatric disorders are outlined in ►**Table 1**, along with the most common symptoms patients may experience.[9] Note the somewhat arbitrary nature of labeling a symptom as "neurological" or "psychiatric."

Creating a space where patients feel supported and do not feel rushed or judged can facilitate the communication of important historical details (e.g., psychotic symptoms, cognitive impairments, suicidal ideation) that patients are otherwise too embarrassed, flustered, ashamed, or anxious to provide. Methods for creating this space may include beginning a conversation with open-ended questions, allowing a patient to speak for several minutes without interruption initially, making good eye contact, and providing nonverbal cues that one is listening (nodding, leaning in) and empathic. Normalizing ("many of my patients with this disease experience this") and validating ("it makes sense you would be experiencing these types of symptoms") comments can put a patient at ease so they will be more inclined to share their true experiences. Additionally, it can help to provide a framework for the interview early to ease a patient's anxiety and to assist them with prioritizing important topics of discussion or concern. For example, a patient who knows that the visit will last approximately 60 minutes and involves a portion of the visit for history-taking and portions for physical exam and treatment planning may be more likely to bring up a concern early rather than waiting until the last 5 minutes. For patients with complex neuropsychiatric symptoms, especially those with significant somatic preoccupation, asking early questions focused on identifying the most bothersome or impairing symptom(s) can narrow the focus of an otherwise potentially unwieldy interview, aligning goals with the patient and improving patient satisfaction, while simultaneously addressing the most cumbersome and time-consuming topics early.

A unique paradox in NP is that an accurate account of the history, often so important to the diagnosis, is also often difficult to obtain. Neurodegenerative disorders affect memory, making it complicated or impossible to get a detailed history directly from the patients themselves. Traumatic brain injury, multiple sclerosis, and epilepsy, among other disorders, can contribute to cognitive impairments. Thus, the involvement of a collateral informant is imperative in most cases. A patient with anosognosia, by definition, cannot appreciate their impairments, and this leads to challenges for health care staff trying to help the patient accept and engage with treatment or therapy recommendations. Moreover, a careful and thorough review of a patient's medical records can offer the most historically accurate longitudinal history as patients engage with a complicated medical system. Sometimes this review can clinch an otherwise unclear diagnosis, especially in the absence of reliable informants. A patient's inability to recount or efficiently relay details of his or her medical history is an important data point for the clinician to synthesize with the remainder of the clinical picture. This could suggest deficits in executive functioning, attention, memory and/or affective regulation or other psychological influences that can be considered as a relevant (albeit nonspecific) data point.

Taking a Neuropsychiatric History—Psychiatric Screening Questions

As psychiatric conditions and dimensional mental health symptoms more broadly are highly comorbid with neurological conditions, it is strongly recommended that a screen for

Table 1 Example of common neuropsychiatric conditions that manifest with both neurological and psychiatric symptomatology

Neuropsychiatric condition	Common "neurological" and cognitive findings	Common "psychiatric" and behavioral manifestations
Alzheimer's disease	Cognitive deficits (memory, orientation, visuospatial processing, executive function), language dysfunction, apraxia, paratonia, myoclonus, word-finding difficulty	Apathy, depression, psychosis (especially delusions of paranoia or spousal infidelity), anxiety, aggression, wandering, confusion, agitation, confabulation, irritability, sundowning, anosognosia
Attention deficit hyperactivity disorder	Inattention, learning problems	Hyperactivity, restlessness, hypertalkativeness, impulsivity, intrusiveness, emotional dysregulation, aggression, low self-esteem, substance abuse
Autism spectrum disorder	Developmental delay, intellectual disability, language impairment, sensory hypersensitivity/intolerance, facial recognition deficits	Social communication deficits, restricted and repetitive behaviors/interests/activities, insistence on sameness, anxiety
Autoimmune encephalitis (especially limbic encephalitis)	Cognitive impairments, involuntary movements, imbalance, speech problems, vision problems, seizures, weakness, paresthesias, headache, fever, nausea, muscle pain, impaired consciousness/coma	Anxiety, panic, sleep disturbances, compulsive behaviors, altered sexual behavior, agitation, euphoria, disinhibition, hallucinations, paranoia
Brain tumors	Weakness, sensory loss, dysphasia, gait disturbance, headache, visual disturbance, seizures, cognitive impairments (confusion, memory loss), papilledema, cranial neuropathies, abnormal motor tone, ataxia, posterior fossa syndrome, nausea/vomiting	Apathy, personality change, palinopsia, psychosis (especially atypical forms such as musical/peduncular hallucinations), pathological laughter, depression, anxiety
CNS infections	Subcortical dementia (inattention, working memory impairment, slow processing speed, language problems), gait abnormalities, ataxia, headache, confusion, seizures, visual disturbances, increased intracranial pressure, nuchal rigidity, disorders of consciousness, dysarthria, fever	Apathy, depression, agitation, disinhibition, psychomotor slowing, psychosis, sleep disturbances, catatonia
Delirium/ Encephalopathy	Inattention (acute onset), other cognitive disturbances (disorientation $\pm$ short term recall deficits), fluctuating course	Sleep disturbances, hyperactive or hypoactive psychomotor activity, hallucinations, agitation, aggression, delusions
Dementia with Lewy bodies and Parkinson's disease	Fluctuating cognition, parkinsonism, movements during REM sleep, cognitive deficits (executive functioning, attention, visuospatial $>$ memory, language), autonomic dysfunction	Visual hallucinations (most common), auditory/tactile/olfactory hallucinations, delusions, sleep disturbances, depression, anxiety, apathy, daytime somnolence, inappropriate sexual behavior
Developmental disorders	Intellectual disability, cognitive dysfunction, motor impairment, language/communication impairment, learning problems	Hyperactivity, impulsivity, social communication deficits, anxiety, sleep disturbances, irritability, anger, dysregulation, aggression, depression, psychosis
Endocrine disorders (Thyroid disease, diabetes, adrenal dysfunction, others).	Cognitive dysfunction (inattention, cognitive inflexibility, slowed processing speed, memory impairments, executive dysfunction), muscle cramps, abnormal reflexes, visual dysfunction, seizures, tremor, myoclonus, ataxia, weakness, impotence	Depression, anxiety, panic, dysthymia, psychomotor slowing, psychosis, mania, fatigue, anergia, decreased libido, sleep disturbances, appetite changes, anger/hostility, irritability
Epilepsy/Seizures	Seizures, intellectual impairment, inattention, memory changes, disorientation, language dysfunction, hyperkinetic or hypokinetic movements, dyspraxia	Affective dysregulation, anxiety, depression (more neurovegetative), apathy, elevated mood, personality change, abnormal perceptions, déjà vu, jamais vu, hallucinations, dysthymia, panic, psychosis, suicidality
Frontotemporal dementia	Language impairment, executive dysfunction, aphasia, dysarthria, mutism, comprehension difficulties, word-finding difficulties	Apathy, disinhibition, loss of sympathy/empathy, impaired affect recognition, perseverative and obsessive-compulsive behaviors, hyperorality, mental rigidity, irritability, aggression, anosognosia

Table 1 (*Continued*)

Neuropsychiatric condition	Common "neurological" and cognitive findings	Common "psychiatric" and behavioral manifestations
Functional neurological disorder	Functional movements, seizures, weakness, speech/voice output difficulties, somatosensory deficits, visual / auditory deficits, cognitive symptoms, pain, fatigue, sleep difficulties	Depression, anxiety (including health anxiety), post-traumatic stress disorder, emotional dysregulation, poor impulse control, coping difficulties, dissociation, alexithymia, maladaptive personality traits
Gilles de la Tourette syndrome	Motor and vocal tics, inattention, learning problems	Depression, anxiety, obsessive-compulsive behavior, hyperactivity
Huntington's disease	Chorea, dystonia, visual disturbances (impaired saccades), gait disturbances, ataxia, dysphagia, dysarthria, athetosis, cognitive impairments (slowed processing speed, memory impairment, executive dysfunction)	Slowed psychomotor speed, apathy, depression, suicidality, irritability, psychosis, anxiety, perseverations, obsessions, compulsions, anosognosia
Hypoxic-ischemic brain injury	Cognitive impairment, movement disorders (parkinsonism, seizures, myoclonus, tremor, dystonia, chorea, athetosis), weakness, coma/disorders of consciousness, akinetic mutism	Anxiety, depression, sleep dysregulation, psychosis, emotional dysregulation
Multiple sclerosis	Paresthesias, weakness, visual disturbances, ataxia, gait disturbances, pain syndromes, spasticity, bladder dysfunction, cognitive dysfunction (slowed processing speed, inattention, poor working memory)	Fatigue, depression, mania, euphoria, pseudobulbar affect, psychosis
Poisons/ Toxidromes	Varied—memory disturbance, cognitive dysfunction, seizures, ataxia, disorientation, inattention, parkinsonism, asthenia	Varied—obsessive-compulsive behavior, depression, rage, impulsivity, amotivation, personality change, fatigue, psychosis, hyperactivity, apathy, restlessness, euphoria, sleep disturbances/nightmares, emotional lability, anorexia
Sleep disorders (narcolepsy, parasomnias, sleep apnea, others)	Cataplexy, movement disorders, seizures, sleep paralysis, movements during rapid eye movement sleep, periodic limb movements, somnambulism, inattention, cognitive impairments	Insomnia, hypersomnia, aberrant nocturnal behaviors, restlessness, mania, irritability, anergia, fatigue, hypnogogic or hypnopompic hallucinations, anxiety, nightmares, depression, PTSD symptoms, panic
Stroke	Hemiparesis, aphasia, hemianopsia, ataxia, vestibular dysfunction, cognitive impairment (slowed processing speed, amnesia), prosopagnosia, anomia, dysarthria, apraxia, spasticity, seizures, coma/disorders of consciousness, akinetic mutism	Psychosis, mania, impulsivity, pseudobulbar affect, irritability, anxiety, depression, apathy, disorganized thought, anergia, sleep disturbance, emotional dysregulation, anosognosia
Traumatic brain injury	Cognitive impairments (inattention, executive dysfunction), motor impairments, oculomotor impairment, cervical strain, sensory impairments, headaches, vestibular dysfunction, aphasia, dysarthria, ataxia, spasticity, seizures, coma/disorders of consciousness, akinetic mutism	Emotional dysregulation, pseudobulbar affect, depression, anxiety, irritability, psychosis, sleep dysregulation, apathy, aggression, fatigue

Abbreviations: CNS, central nervous system; PTSD, post-traumatic stress disorder; REM, rapid eye movement.
Note: The list is not exhaustive but demonstrates the arbitrary nature of separating psychiatric and neurological conditions and their symptom domains. Italicized items are those symptoms traditionally viewed as pathognomic or otherwise critical to the diagnosis of the condition.

common psychiatric conditions and traits be conducted after obtaining a thorough history of the present illness. ►**Table 2** shows an example of some of the most high-yield psychiatric symptom categories to include in the screening, along with some basic lead-in questions to the topic. Although screening for categorical psychiatric diagnoses is important, it is equally important to apply a transdiagnostic approach to screening, emphasizing other areas of psychopathological impairment (e.g., poor impulse control, prominent affective dysregulation) which can present across many diagnoses and impair functioning. It is the synthesis of all this information which guides the provider to a formal diagnosis and clinical formulation.

The psychiatric screen could take 10 to 15 minutes, although the duration is highly dependent on the patient's responses and positive screens that require further elaboration. As many psychiatric conditions are highly treatable and, when untreated, have a significant negative effect on quality

Table 2 Example screening questions for common psychiatric symptom clusters

Neuropsychiatric symptom domain	Screening question examples
Anxiety	Generalized Anxiety: Do you or your friends/family consider you a "worrier"? During the past few months have you frequently been worried or anxious about several things in your daily life? Is your anxiety generally constant or does it come and go based on clear triggers (to distinguish from other anxiety disorders)? Panic: A panic attack is a sudden rush of intense anxiety or fear that can be triggered or come out of the blue, does this ever happen to you? Social anxiety: Some people feel very anxious in social situations, does that ever happen to you? Health anxiety: Some people worry about their health a great deal, so much so that the health worries become a cause of distress themselves, does that ever happen to you?
Cognition	Have you or anyone close to you noticed changes in your memory or thinking? Has anyone mentioned that you have started to repeat the same questions or stories?
Depression	Depressed mood: Over the last 2 wk have you been feeling down, depressed or hopeless? Have you been depressed more days than not over the past 2 y? How is your mood? Anhedonia: Have you lost interest in or get less pleasure from things you used to enjoy? Are there still things you enjoy?
Mania	Have there been times lasting at least several days that you have felt on top of the world or even euphoric, required much less sleep than usual but still had lots of energy? What about several days when you were overly irritable or quick to anger in a way that is unusual for you?
Obsessions and Compulsions	Obsessions: Do you have frequent unwanted thoughts that are hard to control? Compulsions: Some people are bothered by having to repeat activities or rituals over and over, and they can't resist when they try. Have you ever been bothered by something like this?
Personality	General: How would a close family member or friend describe you? Introversion/Extroversion/Novelty-seeking: Are you a "people person" or do you prefer to be alone? In a group are you more quiet or outspoken? Do you often seek out novel or exciting experiences? Impulsivity/Emotional dysregulation: Do you wear your emotions on your sleeve? Are you one to often act without thinking? Do you have a short fuse? Interpersonal: Are you slow to warm up to others? Do you find it difficult to trust people? How would you describe your typical relationships or friendships?
Psychosis	Auditory hallucinations: Have you heard sounds or voices that other people didn't hear? For example, hearing a voice when you were alone in a room? Visual hallucinations: Have you seen visions or seen things that others could not see? Delusions of persecution: How are people here treating you? Is anybody out to get you, monitoring you, following you or trying to hurt you?
Suicidality	Do you ever have thoughts or feelings of wanting to die or wanting to take your own life?
Trauma	Traumatic event: Have you ever had something happen to you that was especially frightening, disturbing, or traumatic? Have you ever witnessed such an event happening to someone else? Hyperarousal: Are you easily startled or "jumpy?" Do you ever have nightmares or intrusive thoughts about the traumatic events you experienced? Avoidance: Do you ever go out of your way to avoid situations, places or people that remind you of the trauma? Dissociation: Do you ever feel numb or detached (disconnected) from people, activities, or your surroundings? Do you ever have out of body experiences or a feeling like your body does not belong to you? Do you have gaps in your memory or periods of time you cannot account for during the day? Re-experiencing/Flashbacks: Do you ever experience a traumatic memory so vividly it feels as if you are reliving the event?

of life and prognosis, it is crucial to incorporate this screening into any neuropsychiatric interview.[10–14] Additionally, neurological conditions can present with a myriad of psychiatric symptoms, some seemingly unrelated; direct questions and prompts can efficiently accomplish this screening while covering many relevant disease categories. Deliberate transition statements when switching between symptom categories can help to re-orient and focus a patient to the task at hand and the provision of useful information (e.g., "I'd like to switch topics for a bit and talk about mood and anxiety symptoms—would that be okay?").

Important concepts to consider in performing a psychiatric screen include:

1. *Acuity and severity*—It is important not to only identify symptoms, but their severity and acuity. This can be assessed by asking about prior need for psychiatric hospitalization, presence of prior or current self-harm or suicidality, and history of previous mental health encounters and treatment trials. It is also important to identify whether the symptoms have significantly interfered with their function either at work or in personal relationships.

2. *Duration*—Many psychiatric diagnoses rely on a longitudinal history to distinguish one from another (e.g., persistent depressive disorder vs. major depressive disorder, PTSD vs. acute stress disorder, etc.). Thus, getting a sense of the duration of symptoms and whether they are persistent or episodic can greatly assist in diagnosis and understanding of whether symptoms represent a manifestation of their neurological condition versus an underlying and premorbid psychiatric condition.
3. Ask about trauma (psychological and physical/TBI), cognitive baseline (often asked as the highest level of education attained or need for special education/individualized education plan in school), and drug and alcohol use (both current and historical). These historical details will color how you view the remainder of the symptoms expressed and can undoubtedly alter the differential diagnosis.[15,16]

In addition to the more classic medical history-taking, it is often helpful to obtain history from patients that gives you a sense of their mental health strengths and their underlying personality. This can provide the clinician with a sense of underlying character traits that may exacerbate symptoms, personality changes that may have occurred with their illness, or psychological stressors contributing to current symptoms. Some good open-ended questions include: (1) "How do you cope with stress?" (2) "Tell me about you as a person before you got sick," and (3) "How would your friends or family describe your personality?" Additionally, for patients who are finding it difficult to organize a chief complaint and/or may be defensive about delving into the psychiatric screening, it can be helpful to perform early social screen (including contextualizing cultural and spiritual factors) as a way of beginning to understand the patient in their context (see social history section for additional details).

Taking a Neuropsychiatric History—Important Details

As alluded to in the previous section, there are certain aspects of a neuropsychiatric history that are crucial for ensuring a complete picture of the patient's situation and which, if missed, can lead to (at best) an incomplete understanding of the patient's clinical picture and (at worst) misdiagnosis and mismanagement, including potential for iatrogenic harm from unnecessary testing or treatment.

Handedness: One aspect of a neurological history that should commonly be obtained is handedness. Handedness is admittedly less important in neuropsychiatric conditions than in disorders characterized by motor or language deficits, although it is good practice to include this information when possible. Handedness not only has implications for brain hemisphere dominance and asymmetric dexterity findings, but may also influence other clinical characteristics such as endocrine reactivity in a way that is poorly understood, yet of interest to the neuropsychiatrist.[17–19]

Developmental history: Another "can't-miss" topic of discussion is developmental history. Asking "what type of student were you in school?" can be illuminating both in terms of intellectual ability and early social and behavioral problems that may point to autism, ADHD, or other neurodevelopmental abnormalities or genetic conditions. Anchoring questions can be helpful, such as asking about how the patient compared with another sibling or whether they met certain developmental milestones (walking at 12–18 months, speaking a few single words at 12–18 months). If a parent is available, questions about the patient's birth history can also be revealing (e.g., APGARs, any indicators of perinatal distress, infection, or bleeding) depending on the differential diagnosis being entertained. This history becomes especially important in patients with long-standing behavioral or psychiatric concerns without clear onset.

Past traumas: A history of psychological trauma and early-life adversity is also an important aspect of a neuropsychiatric history. Adverse childhood experiences are associated with a higher risk for development of a whole host of medical and psychiatric problems,[20–24] and some disorders commonly seen in a NP clinic (functional neurological disorder, dissociative disorders) have a strong relationship with trauma and PTSD.[25–29] Adverse childhood events could include loss of important attachment figures early in life, chronic stress from a lack of nourishment or neglectful care, parental divorce, witnessing parental abuse, and other similar stressors. All these events can potentially have an impact on one's psychological functioning later in life, in addition to the more severe traumatic experiences of physical, sexual, verbal, and emotional abuse, about which psychiatrists often ask. A good non-judgmental lead-in question could be, "What was life like for you growing up?" Specifically asking about trauma and dissociative symptoms is essential, as some patients may otherwise leave this out.

Comorbid medical symptoms: Screening for medical symptoms that often correspond with psychiatric correlates is also high yield. Asking detailed questions about sleep (sleep disorders diagnosed, sleep studies performed, duration of sleep, early morning awakening, parasomnias, REM sleep behavior disorder symptoms, morning headaches, snoring), traumatic brain injuries or concussions in the past (including their severity—amount of time with altered consciousness, duration of post-traumatic amnesia, need for medical intervention or hospitalization, post-concussion symptoms), and details of any neurological conditions can greatly color a clinical picture. For example, REM sleep behavior disorder is highly correlated with the development of Parkinson's disease,[30] and morning headaches or snoring may be a harbinger of underlying obstructive sleep apnea.[31] Sleep apnea is especially important to identify due to its negative impact on mood, energy level, and cognition, as well as its ability to be treated with positive airway pressure devices.[32–34] Traumatic brain injury as well can have a myriad of neuropsychiatric consequences. Sometimes screening for and subcategorizing of these symptom clusters can help coordinate management—TBI patients should be screened for vestibular dysfunction, oculomotor dysfunction, cervical pain and stiffness, headaches/migraines, sleep abnormalities, anxiety and mood disorders, and cognitive complaints as per recent concussion management guidelines.[35] Collateral information is very helpful with these aspects of the history, such as

provided by a bed partner or witness to the brain injury. Neurologists are well-versed in this type of history-taking, although it is worth a reminder to deliberately delve more deeply into these areas of the history due to the high potential for complicating or associating with the neuropsychiatric condition of interest.

A firm grasp of structure–function brain relationships—specifically neuropsychiatric symptoms and their associated localization—can serve the neuropsychiatrist well, especially in the setting of behavioral disturbances from stroke, traumatic brain injury, or neurodegenerative disorders. However, many neuropsychiatric symptoms do not localize to a specific brain region. A great deal of research now focuses on the identification of distributed brain networks or circuits involved in specific human behaviors. This effort has resulted in the conceptualization of symptoms or disorders that may be better explained by circuitopathy or network dysfunction as opposed to regional dysfunction.[36–39] The current scientific understanding of brain networks, including how best to define them and the behavioral implications of their dysfunction, remains a topic of debate and continued research. ►**Table 3** provides a list of neuroanatomical regions organized according to their consensus brain network membership,[40,41] as well as psychiatric symptoms associated with damage or lesioning of each region. Although lesions to the white matter are common and have important clinical implications for disconnection syndromes, relating white matter lesions to specific brain networks is difficult, with some progress in ongoing research efforts.[42–44] For this reason, ►**Table 3** focuses on cortical lesions, though we acknowledge deficits may be due in part to damage to the white matter tracts in proximity to the cortical region.

Table 3 A list of brain regions and their associated neuropsychiatric sequelae following damage or lesioning, based on current state of the knowledge (new functional neuroanatomical relationships are frequently being identified)

Neuroanatomical region—ordered by common brain network affiliation[40,41]	Common neuropsychiatric lesioning effects*
Limbic network and associated structures	
Amygdala	Loss of conditioned autonomic responses, impaired emotional/social decision-making; reduced risk of PTSD after trauma; enlarged in autism; dysfunction can trigger violence Bilateral: Kluver-Bucy syndrome (loss of fear/aggression, hyperorality, hypersexuality)
Anterior cingulate cortex (subgenual component)	Abnormal autonomic responses to emotional experiences, inability to experience and/or regulate emotions, impaired social behavior/judgment; hypoactive in PTSD; improvement in MDD symptoms; dysfunction in schizophrenia
Basal forebrain (ventral striatum)	Severe memory deficits, confusion, inattention, confabulation
Hippocampus/mesial temporal lobe	Left: Amnesia for verbal material (e.g., names) Right: Amnesia for nonverbal or spatial material (e.g., routes) Bilateral: Anterograde memory loss; no effect on procedural memory or remote memory
Hypothalamus	Body temperature dysregulation, altered growth and appetite, dysregulation of water and sodium balance, dysregulated sleep-wake cycles, hypopituitarism, infertility, abnormal breast milk production, fatigue, weakness, anhedonia, visual disturbances, aggression, apathy, hypoactivity
Orbitofrontal cortex	Disruption of social conduct; impaired planning, judgment, decision-making; disinhibition, impulsivity, self-indulgence, childishness, lack of empathy, social inappropriateness, stereotyped mannerisms, narcissism, boastfulness, callousness, inability to grasp context of complex situations (e.g., Phineas Gage)
Septal nuclei	Rage, aggression (stimulation inhibits aggression, induces pleasure)
Temporal Pole/anterolateral temporal lobe	Left: Impaired retrieval of proper nouns Right: Impaired retrieval of concepts for unique entities, loss of retrograde episodic and declarative knowledge
Somatomotor and auditory networks	
Frontal premotor region	Apraxia
Frontal primary motor area	Contralateral hemiparesis
Frontal supplementary motor area	Akinetic mutism, +/− weakness

Table 3 (*Continued*)

Neuroanatomical region—ordered by common brain network affiliation[40,41]	Common neuropsychiatric lesioning effects*
Somatosensory cortex	Disrupted tactile perception
Superior temporal gyrus	Bilateral: Pure word deafness Left: Fluent aphasia (posteriorly)
Subcortical and noncortical structures	
Cerebellum	Gait ataxia, ipsilateral dysmetria, dysarthria, oculomotor issues; cognitive-affective cerebellar syndrome (executive dysfunction, verbal/visual memory problems, aprosodia, anomia, agrammatism, speech latency, brief speech responses, oral motor apraxia, motor delay, dyslexia, blunted affective, disinhibition, irritability, social/emotional dysfunction, perseveration, inattention, hyperactivity)
Midbrain and brainstem	Cranial neuropathies, loss of consciousness / impairment of arousal, hemiparesis, sensory disturbances, peduncular hallucinosis, vestibular and cerebellar symptoms
Thalamus	Anterior nucleus: Word-finding deficits, confrontational naming deficits, semantic paraphasias (L > R), amnesia, confabulation, palipsychism/perseveration, apathy, visuospatial deficits (R-sided lesion), lack of spontaneous speech (L-sided lesion) Dorsomedial nucleus and mammillary bodies: Severe anterograde amnesia, confabulation, retrograde amnesia with temporal gradient, disturbed problem-solving, apathy, amotivation fluctuating with disinhibition, psychosis, mania, decreased level of consciousness, vertical gaze paresis, cognitive impairments Inferolateral thalamus: Ataxia, hypoesthesia, dysexecutive symptoms Posterior thalamus: Hypoesthesia, homonymous horizontal sectoranopia
Task negative network regions (e.g., Default mode network)	
Frontopolar and medial prefrontal cortex (Dorsomedial and ventromedial)	Social cognition impairments, impaired multi-tasking, executive dysfunction, impaired set shifting, impaired emotion awareness / expression, normal neuropsychological testing other than difficulties with Wisconsin card-sorting test and set-shifting tasks, impaired self-referential thought and reduced mind-wandering
Inferior parietal lobe (Posterior component)	Impaired recall of autobiographical memory, apraxia, contralateral hemi-neglect (right hemisphere), anosognosia
Inferior temporal lobe	Left: Anomia for non-unique entities, common nouns Right: Impaired retrieval of concepts for non-unique entities
Precuneus	Impaired egocentric object localization, impaired visual attention
Task positive network regions (e.g., Frontoparietal, dorsal attention, salience / ventral attention)	
Angular gyrus	Left: Dyscalculia, dysgraphia, finger agnosia, left-right confusion (Gerstmann's syndrome), contralateral hemianopia, lower quadrantanopia, directional hypokinesia Right: Topographic memory loss, anosognosia, construction apraxia, dressing apraxia, contralateral hemi-neglect, contralateral hemianopia, lower quadrantanopia, directional hypokinesia
Anterior cingulate cortex (dorsal component)	Apathy, abulia, akinetic mutism, blunted affect, impaired error detection, emotional instability, inattention, improvement in OCD symptoms
Anterior insula	Anterior: Autonomic dysregulation, impaired perceptual processing (auditory, gustatory), altered pain processing,

(*Continued*)

Table 3 (*Continued*)

Neuroanatomical region—ordered by common brain network affiliation[40,41]	Common neuropsychiatric lesioning effects*
	cognitive control abnormalities, loss of libido, apathy, inability to recognize disgust, amotivation, fatigue, motor impairments Right: Impaired somatosensory function and impaired body awareness Left: Language dysfunction, immediate and delayed memory deficits, aphasia
Dorsolateral prefrontal cortex	Delayed responding but preserved decision-making, intelligence deficits, loss of fluency, perseveration, set-shifting difficulty Left: Verbal working memory deficits, depression Right: Spatial working memory deficits, mania
Frontal eye field	Ipsilateral conjugate gaze deviation (gaze directed toward the lesion)
Frontal operculum	Left: Non-fluent aphasia, long response latency, loss of prosody, slowed speech, grammatical errors, phonemic paraphasias, impaired repetition, impaired naming and writing, impaired verb retrieval Right: Loss of prosody, gesturing, affect, paralinguistic communication deficits
Superior parietal lobule	Agraphesthesias, astereognosis (right or left), optic ataxia Right: Contralateral hemi-neglect and hemi-inattention, anosognosia (unaware of deficit), anosodiaphoria (unconcerned with deficit), constructional apraxia Left: Ideomotor apraxia
Supramarginal gyrus	Conduction aphasia (if arcuate fasciculus deep to cortex is damaged); repetition and naming deficits
Temporoparietal junction	Left: Fluent aphasia (paraphasic speech, phonemic and semantic paraphasias, impaired repetition, defective aural comprehension) Right: Amusia (impaired music processing), phonagnosia (loss of voice recognition) Bilateral: Auditory agnosia (cannot recognize speech or sound), impaired self-other discrimination
Ventrolateral prefrontal cortex	Emotion dysregulation, behavioral dyscontrol, motor response disinhibition
Visual network	
Dorsal Occipital Lobe (occipitoparietal)	Bilateral: Visual disorientation (simultanagnosia), ocular apraxia (visual scanning deficit, psychic gaze paralysis), optic ataxia (impaired visually guided reaching) (i.e., Balint's syndrome); astereopsis (loss of depth perception); loss of motion perception
Mesial Occipital Lobe (primary visual cortex)	Contralateral visual field cut (hemianopsia) with macular sparing Bilateral: Cortical blindness
Occipitotemporal junction	Bilateral: Visual associative agnosia (loss of meaning of image); prosopagnosia (bilateral or right hemisphere lesion primarily) Left: Impaired letter or word recognition
Ventral Occipital Lobe (occipitotemporal)	Contralateral achromatopsia and visual field cut (hemianopsia) Left: "Pure" alexia, impaired mental imagery, color anomia Right: Apperceptive visual agnosia, loss of facial imagery Bilateral: Visual object agnosia, prosopagnosia

Abbreviations: MDD, major depressive disorder; OCD, obsessive-compulsive disorder.
Note: Many neuropsychiatric symptoms fail to localize to any specific brain region but may still localize to a common network of brain regions. This table assumes left-hemisphere language dominance in reporting lateralized findings.

Cognitive symptoms: A screening for cognitive symptoms is foundational to NP. Cognitive complaints should be characterized (with emphasis on potential localizing characteristics of the complaint, again see ►**Table 3**) in detail. Important information includes examples of reported challenges and their context, duration of symptoms, and progression over time. Cortical localizing symptoms (aphasia, visuospatial dysfunction, and amnesia) are important to distinguish from subcortical findings (impaired processing speed, and inattention) as this can have a bearing on diagnostic considerations. Involvement of a caretaker or family member is again imperative for obtaining an accurate account. Impairment of instrumental activities of daily living is the criterion that distinguishes dementia from mild cognitive impairment. Therefore, questions about patients' ability to manage activities independently (finances, driving, socializing appropriately, shopping, cooking) should be explicitly detailed. Often, questions about day-to-day functioning can segway nicely into a more thorough and extensive psychosocial assessment.

Psychosocial Assessment

A complement to the history-taking on daily functioning is the psychosocial assessment. This can be considered an extended social history, providing a more in-depth understanding of the patient's social situation, stressors, supports, and home environment. These details are crucial for engaging the necessary supports in carrying out treatment planning, as well as for gaining a better understanding of available family assistance or challenges that could make the patient's clinical course more or less stable than otherwise expected. Having completed much of the history of present illness, a good transition question may be along the lines of "How has this disease [or symptom(s)] affected you in your life?" This gives the provider a sense of activities that are meaningful to the patient and how they view their situation and degree of impairment. Usual social history information about the patient's vocation and job responsibilities, financial status, upbringing and household structure, and quality of relationships can all be telling information to better grasp the patient's level of functioning, available resources, and interpersonal qualities. Identification with specific ethnic, cultural, or spiritual groups can also prove to be valuable information for understanding potential beliefs that may color patients' experiences or interpretation of their illness. In addition to current social history, relationship and work history can provide insight into the longitudinal trajectory of their functioning. Knowledge of disability status (including whether they are actively seeking disability) is a good metric of level of dysfunction and disease impact.

Level of education completed and involvement in special education classes give a sense of the patient's cognitive capacities at baseline and may help guide the degree of complexity with which the clinician delivers medical information and recommendations. Other useful areas to cover include asking about one's coping strategies for stress, how he or she interprets the current situation (insight), and how "psychologically-minded" he or she is (i.e., the ability to identify emotions and introspect about their situation). All these factors will play a role in the development of a comprehensive and individualized assessment and treatment plan.

Additionally, it is often important to understand how the disease has impacted the patient's close family, and the structure of their support system. A patient with early signs of cognitive impairment with a healthy, supportive spouse and adult children may have a very different prognosis than a similar patient who is homeless or living alone with no close family. It is also clear that family members of patients with brain injury or neurodegenerative illness are at high risk for development of caregiver burnout or mental health disorders themselves.[45–47] Remaining vigilant to the struggles of the patient's primary caretakers is thus essential to the provision of good care to the patient. Evidence of burnout in caregivers should be managed aggressively by seeking social work assistance or caregiver respite to find additional support when possible, or to begin discussions about the need for and timeline to patient placement. Personality changes have been identified as the most stressful aspect of neurological disorders for caregivers,[45] and thus caregivers presenting with patients in the NP clinic are often those at the highest risk for burnout and mental illness themselves.

Atul Gawande recently wrote a book entitled *Being Mortal*,[48] which focuses on the importance of discussions surrounding end-of-life care to ensure patients maintain dignity and optimize their quality of life in the face of terminal illnesses. Some of the discussion questions Dr. Gawande suggests in his book can be directly applicable to patients with neuropsychiatric disorders, especially those with chronic conditions. These questions are thoughtful methods for getting high-yield conversations started with patients and their families, and include:

1. What are your fears and worries for the future?
2. What are your goals and priorities?
3. What outcomes are unacceptable to you? What are you willing to sacrifice and not?
4. With your current condition, what would a good day look like for you?

Depending on the specifics of a given case, some of these questions may be good to ask about in follow-up—with a framing that one's evaluation of the patient occurs both cross-sectionally and longitudinally.

Family History

Taking a family history can be a useful, albeit imprecise, method for understanding the genetic vulnerabilities in specific families. Neurological and psychiatric conditions each carry a different degree of heritability (see ►**Table 4** for heritability measures of common neuropsychiatric diseases) and in many cases family members may go without a formal diagnosis. Some clinicians have found that person-focused history-taking ("did your mother have any neurological or psychiatric conditions? Did your father…?") as opposed to disease-focused family history ("did anyone in

Table 4 Heritability of various neuropsychiatric conditions, with other traits as points of reference

Neuropsychiatric condition	Heritability approximations
Huntington's disease	100%
Bipolar disorder[95]	85–89%
Autism spectrum disorder[96]	83–87%
Schizophrenia[97]	73–90%
Gilles de la Tourette syndrome[98]	70–85%
Human height (trait for reference)[99]	68–93%
Attention-deficit hyperactivity disorder[100]	68–76%
Alzheimer's disease[101]	60–80%
General cognitive ability (IQ)[102]	approximately 62% (20–80% depending on age)
Parkinson's disease[103]	50–70%
Multiple sclerosis[104]	39–61%
Narcolepsy[105]	35–39%
Dementia with Lewy bodies[106]	31–60%
Major depressive disorder[107]	31–42%
Epilepsy[108]	24–41%
Glioma[109]	20–31%
Obstructive sleep apnea traits[110]	17–70%
Ischemic stroke[111]	16–40%

Note: Heritability refers to the proportion of trait variance or disease liability that is due to genetic factors, or put more simply, how well differences in genes account for differences in their risk of a given disorder. A heritability value close to 100% indicates that almost all the variability in a diagnostic phenotype comes from genetic variance, with very little contribution from environmental factors. Notably, many neuropsychiatric disorders are the product of gene–environment interactions.

the family have dementia?") may be higher yield by focusing the patient's thoughts more deliberately. Additionally, obtaining history about family members who may have had symptoms without a diagnosis can be a useful skill—often asking about estranged family members, difficult or "bizarre" family members, or those with a history of incarceration or substance use can provide clues as to diseases or personality traits that run in the family.

Neuropsychiatrically-Informed Neurological and Mental Status Exam

The details and nuances of the neurological exam are beyond the scope of this paper and have been reviewed extensively elsewhere.[49] However, a thorough screening of the patient's central and peripheral nervous systems is critical, including a mental status exam, cranial nerve inspection, motor exam, reflexes, sensory exam, cerebellar function interrogation, and gait exam. Two neurological exam features of specific interest to neuropsychiatrists are positive signs of functional neurological disorder and neurological "soft signs." "Soft signs" are subtle neurological impairments in sensory perception and integration, motor coordination, and sequencing of complex motor acts which are non-focal and non-specific, although pathologic and suggestive of underlying brain dysfunction. They are commonly seen in psychotic disorders and other non-localizing neuropsychiatric pathologies.[50] These unique components of the neurological exam are reviewed in other publications.[51–55] Positive signs of functional neurological disorder are useful for "ruling in" this diagnosis and include techniques such as the Hoover sign, the hip abductor sign, and tremor entrainment. Frontal release signs are examples of neurological soft signs which can be used to identify patients with frontal lobe impairment, indicating the re-emergence of primitive reflexes with loss of frontal cortex inhibitory processes. These may be an indication of a neurodegenerative process or traumatic brain injury. Frontal release signs include glabellar tap, jaw jerk, palmomental reflex, corneomandibular reflex, pout and snout reflexes, grasp reflex, and forced groping.

The mental status exam is often considered the "physical exam" of psychiatry and can usually be incorporated into the neurological exam and history, as it involves many observational components as well as some bedside cognitive screening. The components of the mental status exam are outlined below, as well as examples of abnormal findings for reference.

General appearance, behavior, and attitude: Disorganized or cognitively impaired patients may be disheveled or demonstrate poor self-hygiene. Non-dominant parietal lobe lesion patients may present with poor self-care primarily on the left side of the body (hemi-inattention). Patients with persecutory delusions or paranoia may be guarded and may distrust the examiner. Some patients with dementia may appear pleasantly confused without specific complaints. Patients with frontotemporal dementia may exhibit disinhibited or impulsive/repetitive behaviors. Patients with psychosis may appear distracted, whispering to themselves, or preoccupied. Patients with depression or anxiety may make poor eye contact and show psychomotor activity changes (fidgety or bradykinetic). Commenting on the presence or absence of abnormal motor movements (tremor, tics) is also useful. Patients suffering from catatonia will demonstrate severe bradykinesia or psychomotor agitation, posturing, grimacing, staring, and a host of other observable motor symptoms.

Speech: Patients with Parkinson's disease may have hypophonic speech or increased speech latency. Patients with cerebellar damage may demonstrate scanning speech and abnormal speech rhythm. Patients with right hemisphere lesions may have loss of prosody. Expressive aphasia patients present with hesitant and halting speech. Apraxia of speech can be a sign of dominant hemisphere stroke or neurodegenerative disorder, such as primary progressive aphasia.

Flow of thought: Patients with advanced dementia will likely demonstrate perseverative speech. Frontotemporal

dementia patients are often stimulus bound and thus tangential and distracted by stimuli in the environment. Elderly patients, especially those with mild cognitive impairment, may demonstrate circumstantial flow of thought. Patients with receptive aphasia or certain forms of primary progressive aphasia may demonstrate speech that borders on word salad (extremely disorganized or unintelligible speech consisting of seemingly random words and phrases).

Content of thought/Associations: Important considerations include presence or absence of persecutory delusions (common in Alzheimer's dementia, especially persecutory delusions such as delusions of theft or spousal infidelity/Othello syndrome),[56] perceptual distortions, such as visual hallucinations (oftentimes a sign of Parkinson's disease psychosis or Lewy body dementia), somatic preoccupations, suicidality, homicidality, self-harm urges, obsessions, feelings of guilt or hopelessness.

Mood: Oftentimes this is just a quote of the patient's subjective mood state. Represents the internal experience of the patient.

Affect: The outward appearance of the patient's positive and negative valence systems. Often described as euthymic, hyperthymic, or dysthymic, with comments on the range of affect (labile, constricted, blunted, etc.). Patients with right hemisphere lesions may present with limited range of valence or inappropriate valence to the content of conversation; others may experience post-stroke mania and labile affect[57] or post-stroke depression with restricted affect.[58] Some patients with neurodegenerative disorders or traumatic brain injury may experience pathological laughing and crying.[59]

Insight and judgment: Insight refers to a patient's ability to introspect about their own condition and the implications of their condition within their personal life situation. Patients with anosognosia from a non-dominant hemisphere lesion often lack insight, as do patients with more advanced forms of amnestic dementia. Lack of insight in neuropsychiatric illnesses can be a poor prognostic factor.[60–62] Judgment refers to the patient's ability to comprehend information, rationally manipulate that information, and then apply that information to make decisions about one's condition or situation. Lack of judgment can be seen in patients with ventromedial prefrontal or orbitofrontal brain lesions, frontotemporal dementia, or severe forms of depression and psychosis.

Sensorium and intellect: Sensorium and intellect refer to the mental status equivalent of bedside cognitive testing. Cognitive domains which can be quickly tested at the bedside include orientation, short-term recall, attention and concentration, language, executive function, calculations, abstraction, visuospatial function, and fund of knowledge. Based on the pattern of cognitive domains affected in any given patient, an astute neuropsychiatrist can begin to develop a differential diagnosis of potential contributing or causative factors or diseases. For example, a patient with disorientation may be presenting with encephalopathy/delirium, intoxication, or Lewy body dementia, depending on the circumstances. Significant challenges on short-term memory testing accompanied by executive dysfunction on a clock-drawing task and circumlocutions or word-finding challenges on a language task may support an amnestic variant of Alzheimer's disease pathology as the leading diagnosis on the differential. Later sections will discuss additional tools for bedside cognitive testing, as well as their advantages and disadvantages. A full discussion of the implications of neuropsychological testing abnormalities and patterns is beyond the scope of this paper, and has been reviewed elsewhere.[9,63]

Psychiatric Assessment Tools and Symptom Scales

Psychiatric assessment tools are frequently employed in NP for three primary goals: (1) screening, (2) diagnostic aid, and (3) symptom and outcome monitoring. Tools can provide a standardized method for both capturing and quantifying disease characteristics that may be difficult for patients to articulate or which may manifest in unique ways from one patient to the next. They can be especially helpful as a baseline assessment to screen for specific symptoms or diagnostic categories, or to support a suspected diagnosis from clinical interview. Another common use is for tracking symptoms over time, such as during a treatment trial, or to get a better sense of the trajectory or longitudinal course of a problem (e.g., are symptoms waxing and waning? persistent and unchanged? gradually worsening?). Scales can often be administered quickly while a patient is in the waiting area, or potentially even sent to the patient electronically prior to an appointment for completion. A list of commonly used scales based on the neuropsychiatric metric of interest are outlined in ►**Table 5**. For general assessment of depression and anxiety levels, the combination of PHQ-9 and GAD-7 can provide valuable information in a short time. The Quality of Life in Neurological Disorders (Neuro-QoL) and the PROMIS questionnaire are rapid, flexibly administered screening metrics developed by the U.S. Department of Health and Human Services which provide measures of physical, mental, and social health more broadly.

Bedside Cognitive Screening Tools

Psychiatric assessment tools often measure some aspect of the affective or motivational systems in the brain. The cognitive correlate of this is the bedside cognitive assessment. Psychiatrists and neurologists are trained in performing a bedside cognitive assessment, the details of which are beyond the scope of this review. However, oftentimes it can be useful to employ a cognitive screening tool to get a more standardized assessment of a patient's cognitive functioning. Although these rapid bedside or clinic-based tests often lack specificity when it comes to diagnosing mild cognitive impairment, they can provide valuable information regarding a patient's functioning across relevant cognitive domains and provide some guidance to clinicians on when a patient may require more thorough neuropsychological testing performed by trained psychologists or psychometricians. Two of the most common bedside cognitive tests are the Mini Mental Status Exam (MMSE) and the Montreal Cognitive

Table 5 Commonly used clinical scales to assess various neuropsychiatric symptom domains and severity, or associated traits of relevance

Neuropsychiatric domain	Tool/Instrument
General assessment	Brief Psychiatric Rating Scale (BPRS) Brief Symptom Inventory 18 (BSI-18) DSM-5 Self-Rated Cross-Cutting Symptom Measure Neurobehavioral Rating Scale (NBRS) Neuropsychiatric Inventory (NPI)
Anxiety	Anxiety Sensitivity Index Beck Anxiety Inventory (BAI) Generalized Anxiety Disorder-7 (GAD-7) Hamilton Anxiety Rating Scale (HAM-A) Hospital Anxiety and Depression Scale (HADS) State-Trait Anxiety Inventory (STAI)
Apathy	Apathy Evaluation Scale (AES) Apathy Inventory (AI)
Depression	Beck Depression Inventory (BDI-II) Center for Epidemiological Studies Depression Scale (CES-D) Epilepsy (NDDI-E) Geriatric Depression Scale (GDS) Hamilton Depression Rating Scale (HAM-D) Inventory of Depressive Symptomatology (IDS) Montgomery-Asberg Depression Rating Scale (MADRS) Neurological Disorders Depression Inventory in Patient Health Questionnaire (PHQ-9) Quick Inventory of Depressive Symptomatology (QIDS)
Dissociation	Dissociative Experiences Scale (DES-II)
Impulsivity	Abbreviated Impulsiveness Scale (ABIS)
Involuntary movements/tics	Abnormal Involuntary Movements Scale (AIMS) Barnes Akathisia Scale (BAS) Premonitory Urge for Tics Scale (PUTS) Tic Symptom Self Report Scale (TSSR) Yale Global Tic Severity Scale (YGTSS)
Mania/Bipolar spectrum	Mood Disorders Questionnaire (MDQ) Young Mania Rating Scale (YMRS)
Obsessions and compulsions	Obsessive Compulsive Inventory (OCI) Yale-Brown Obsessive-Compulsive Scale (Y-BOCS)
Panic	Panic Disorder Severity Scale (PDSS) Panic and Agoraphobia Scale (PAS)
Personality and temperament	Adult Temperament Questionnaire (ATQ) Minnesota Multiphasic Personality Inventory (MMPI) Temperament and Character Inventory (TCI)
Psychosis	Positive and Negative Syndrome Scale (PANSS) Psychotic Symptoms Rating Scale (PSYRATS) Scale for Assessment of Positive Symptoms (SAPS)
Quality of life	EuroQol-5D (EQ-5D) Quality of Life in Epilepsy (QOLIE-31) Short Form Survey Instrument (SF-6D, SF-36)
Sleep	Epworth Sleepiness Scale (ESS) Pittsburgh Sleep Quality Index (PSQI)
Suicidality	Beck Scale for Suicide Ideation (BSI) Columbia-Suicide Severity Rating Scale (C-SSRS)
Trauma related	Clinician Administered PTSD Scale (CAPS) Mississippi Scale for Combat-Related PTSD (M-PTSD) PTSD Checklist for DSM-5 (PCL-5) Treatment-Outcome PTSD Scale (TOP-8)

Note: This list is a representative example but is not exhaustive.

Table 6 Domains of cognitive function and bedside screening tools and tests which assess them

Cognitive domain	Bedside screening tools and tests
Attention and concentration	BoCA—mental math MMSE—"WORLD" backward MoCA—serial 7s, digit span, sustained attention to list of letters SLUMS—digit span
Executive functioning	BoCA—clock test Go/No-Go Task (response inhibition) Luria Motor Sequence (motor set shifting) Mini Cog—clock drawing MoCA—trails, clock drawing, phonemic fluency, abstraction— RUDAS—judgement SLUMS—shape comparison, story
Language	BoCA—identifying objects/prefrontal synthesis, naming, repetition, reading, spelling MMSE—naming MoCA—naming, repetition SLUMS—naming
Memory	BoCA—registration and delayed recall, semantic knowledge Mini Cog—registration and delayed recall MMSE—registration and delayed recall MoCA—registration and delayed recall, naming (semantic knowledge) RUDAS—registration and delayed recall SLUMS—delayed recall
Orientation	BoCA, MMSE, MoCA, RUDAS, SLUMS
Praxis	RUDAS—copy actions
Visuospatial functioning	BoCA—mental rotation Clock Drawing Test Mini Cog—clock drawing MMSE—intersecting pentagons MoCA—trails, cube drawing, clock drawing RUDAS—body orientation, cube drawing SLUMS—clock drawing, shapes

Abbreviations: BoCA, Boston Cognitive Assessment;[114] MMSE, Mini-Mental State Exam; MoCA, Montreal Cognitive Assessment; RUDAS, Rowland Universal Dementia Assessment Scale[112]; SLUMS, St. Louis University Mental Status.[113]

Assessment (MoCA), which will be briefly discussed here. A list including these and other cognitive screenings, including which cognitive domains they can be useful for evaluating, is outlined in ►**Table 6**. Some scales are designed to evaluate for distinct neuropsychiatric disorders, such as the Cerebellar Cognitive Affective Syndrome Scale[64]—detailed discussion of disease-specific cognitive screenings is beyond the scope of this manuscript.

Mini-Mental Status Exam[65]: The MMSE is a 30-item scale which takes approximately 5 to 10 minutes to administer. A score of 24 or greater is considered within a normal range, whereas lower scores suggest cognitive impairment that should be further evaluated.[66] This scale can also be used to track cognitive performance over time, with changes of 1 to 5 points between administrations considered a significant degree of change.[67,68]

Considerations for clinicians: This scale is easy and fast to administer, and it is widely used across the world to provide a reasonably comprehensive cognitive screening. Some weaknesses include the fact that it does not consider level of educational attainment in the score (which is associated with performance,[69] leading to a high false-negative rate in highly educated individuals and a high false-positive rate in those with minimal formal education), it relies heavily on language function for its tests, and it does not have a measure of executive function, which is often a highly relevant cognitive domain for the neuropsychiatric exam. Additionally, the MMSE is copyrighted and thus there is a cost associated with every use.

Montreal Cognitive Assessment[70]: The MoCA is also a 30-item scale. It takes approximately 10 minutes to administer, slightly longer than the MMSE, depending on patient performance. Scores of 18 to 25 have been associated with mild cognitive impairment, whereas scores in the 10 to 17 range have been associated with moderate dementia. However, score cut-offs to best separate normal functioning from mild cognitive impairment vary: one study showed that a score less than 23 was more sensitive and specific for identifying patients with mild cognitive impairment from Alzheimer's disease,[71] whereas another identified scores less than 17 as the most sensitive cut-off for MCI.[72] A significant change with repeat testing is usually on the order of four points per year.[73] Additionally, scores on the MOCA (or other bedside cognitive tests) should not be used in isolation, as the complete clinical picture helps put the clinical score in context.

Considerations for clinicians: Compared with the MMSE, the MoCA has less of a ceiling effect, as it is somewhat more challenging. It factors in a score adjustment based on one's

level of educational attainment, and it also includes some measures of executive functioning.

For the clinician pressed for time, the Mini-Cog is a concise, 3 to 4 minutes bedside test consisting solely of a three-word recall test and a clock drawing task.[74] Some studies have shown this to have reasonable sensitivity and specificity (76 and 89%), on par with the MMSE for detecting mild cognitive impairment or dementia.[75,76] Additionally, it appears to have less variability based on patient age or educational background.[77] Although it sacrifices the ability to assess a wider range of cognitive domains, the Mini-Cog may have a place in the busy primary care, specialty care, or hospital setting.

Laboratory and Diagnostic Testing

After completing a comprehensive neuropsychiatric history, targeted physical and neurological exam, and adjunctive symptom quantification with validated psychometric assessment tools for behavioral and cognitive symptoms as needed, the final step in the neuropsychiatric evaluation is thoughtful ordering and interpretation of relevant diagnostic testing. This may include laboratory tests of serum and cerebrospinal fluid, electroencephalography, brain and spinal cord imaging, autonomic testing, electromyography, and nerve conduction studies. Often, these tests are used to rule in or out potential causes for the neuropsychiatric symptom in question—for example, is the patient's new cognitive complaint evidence of a neurodegenerative disorder (evaluated with structural neuroimaging and potentially amyloid or tau PET scan, CSF amyloid β-42, and tau concentrations), or could it be related to a seizure disorder (evaluate with EEG), a brain tumor (ruled out with brain imaging), a thyroid problem (evaluated with thyroid stimulating hormone and free T4 serum levels), or a mood disorder? It is important to remember to order tests judiciously and to understand the rationale for targeted testing—for example, studies have shown that rates of fatigue, depression, and anxiety in subjects with overt or subclinical hypothyroidism are similar to euthyroid subjects, which may draw into question the utility of this test for subjects presenting with fatigue or mood complaints.[78,79] However, this finding has not been universal, and other carefully conducted studies have found subtle deficits in memory and executive functioning even in subclinical hypothyroidism populations.[80] This nuanced knowledge of the tests ordered will, at a minimum, afford the clinician greater skill at interpreting the results in the context of the clinical picture. Similarly, it is important to remember the sensitivity and specificity of the tests being ordered—for example, a single routine EEG has a sensitivity ranging from 25 to 56% and specificity from 78 to 98% as a diagnostic test for epilepsy.[81] One can only approach a greater level of certainty "ruling out" an epileptic seizure disorder by capturing the events or symptoms on a video EEG, or by repeated negative routine EEGs (sensitivity peaks at 82 to 92% with little additional diagnostic yield beyond four routine EEGs, especially if activation procedures are involved).[82–84] In addition to understanding the "hit rate" of a test and exactly what information you can learn from it, NP providers should always ask themselves how the results of a test may change their management. If the test will not change management or provide some additional useful information for treatment planning or prognosis, it is worth questioning whether to use resources obtaining it. A discussion of specific diagnostic tests and their utility is beyond the scope of this manuscript.

When to Order Imaging

One of the most common questions which arises during the neuropsychiatric work-up is when to order a brain MRI or CT scan. This is a complex question, and the answer is likely to require an individualized decision based on several patient factors. Again, we can think about "hit rates" for imaging studies in patients with psychiatric conditions as a good indicator of the benefit versus cost in general. One study of 2,922 psychiatric patients at a single site showed that 31.8% had "relevant pathology" identified on imaging, with a greater chance of pathology seen in patients with dementia, head trauma, or older age.[85] "Relevant pathology" in this study, however, did not necessarily mean actionable findings—white matter hyperintensities and similar findings were included in the "hit rate" due to their potential relevance for psychiatric pathology, despite the chance that it would not change patient management. Indeed, other studies of imaging in first-episode psychosis or schizophrenia patients show significant rates of incidental findings (16–31%) but only a small percentage of those required additional medical referral or attention (2.3–10.3%).[86,87] This is not all that different than the "hit rates" in healthy control subjects—one NIH study showed that in a sample of 1,000 healthy subjects, the rate of incidental MRI findings was 18%, with only 2.9% requiring additional medical attention.[88] The American Psychiatric Association guidelines, therefore, suggest structural neuroimaging for first-episode psychosis patients only if clinically indicated by an unusual pattern of illness or neurological signs, or if the imaging is expected to alter diagnostic or treatment-related decision-making. Similar guidelines have been adopted by the United Kingdom, Canada, and New Zealand.[89] However, other countries' guidelines, such as the 2016 Australian Orygen guidelines, recommend neuroimaging in cases of first-episode psychosis. Thus, expert consensus varies.

When to order imaging on patients with neuropsychiatric disorders differs from other psychiatric work-ups in that most patients have had previous head imaging from their neurological diagnostic work-up. Nonetheless, two good rules of thumb are to order imaging when there is (1) a new neurological problem or (2) a change in the character, intensity, or quality of a previously existing neuropsychiatric symptom. Although indications for neuroimaging in psychiatric presentations have been proposed in the past,[90] we propose in ►**Table 7** a list of "red flag" symptoms for a neuropsychiatric patient which may warrant further neuroimaging evaluation (assuming some level of baseline imaging exists from previous historical work-ups).

Similar questions also often arise for ordering an EEG on a patient, with similar themes and conclusions. In patients

Table 7 "Red Flag" symptoms which may indicate need for repeat diagnostic neuroimaging in neuropsychiatric patients

New onset psychiatric symptoms with pre-existing neurological condition or brain pathology, if an acuity or severity consistent with or suspicious for underlying neurological decompensation
Significant change in presentation of neurological signs or symptoms
Recent head injury or suspected head injury with *change in neurological or psychiatric status*
Epileptic seizures (especially *new onset or change* in character or frequency)
Acute onset of delirium or altered mental status
Cognitive impairment concerning for dementia (to rule out microhemorrhages and to evaluate pattern of focal/lobar atrophy)
Pre-surgical or pre-procedural planning for various neuropsychiatric conditions and interventions (for example, epilepsy surgery, deep brain stimulation, electroconvulsive therapy)

Note: This study assumes that baseline diagnostic imaging has already been obtained historically; otherwise may be appropriate to obtain a baseline scan on almost any patient who presents with new onset of combined neurological and psychiatric symptoms. Note the pattern of ordering imaging in the setting of a new symptom or significant change in symptoms. Please note, these are general guidelines and cannot replace a clinician's astute medical decision-making and weighing individual patient factors unique to each case.

with psychiatric conditions, the detection rate of abnormal EEG findings is significant (17.6–31%)[91,92] but the presence of actionable findings that changed diagnosis was low (1.7% in one study)[92] and only slightly higher than the rate of epileptiform activity identified in healthy individuals (0.5% in one study screening aircrew training program participants).[93] Indications for EEG are well-described elsewhere and may include concern for new psychiatric or neurological symptoms in a patient with known epilepsy; atypical neuropsychiatric symptoms suspicious for epilepsy (atypical hallucinations such as unilateral hallucinations, atypical panic attacks, dissociative symptoms, repetitive aggressive episodes without clear motivation, or medically unresponsive ADHD); evaluating acute confusion in the absence of a medical explanation; evaluating suspected encephalitis or encephalopathy; and history of a significant brain insult such as TBI or stroke.[94]

Conclusion

The neuropsychiatric assessment can be complex and challenging to perform for the untrained clinician. The assessment often requires sifting through a broad differential and dense medical history with nuanced questioning, then developing an individualized treatment plan with patient and caregiver buy-in. It is complicated in many cases by patients who are trying to organize and relay information through the diseased organ in question, as well as caregivers providing histories often understandably influenced by frustration, embarrassment, fatigue, and bewilderment.

Here, we attempted to provide special focus on the unique aspects of the neuropsychiatric assessment that set it apart from other standard medical history-taking and assessment details. We also attempted to distill the information into clinically relevant and focused subsections for broad applicability to medical providers who frequently encounter patients suffering from neuropsychiatric symptoms, potentially serving as a refresher for neuropsychiatrists and behavioral neurologists, and more importantly as a primer for primary care clinicians, general neurologists and psychiatrists, as well as subspecialty trained neurologists. As the prevalence of neurodegenerative diseases continues to grow, clinicians and educators in NP and BN need to develop methods to train other medical professionals to assist in the management of this growing set of patient populations. We hope this article and others like it can bridge the care gap and enable high-quality integrated and patient-centered care for patients with brain diseases.

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