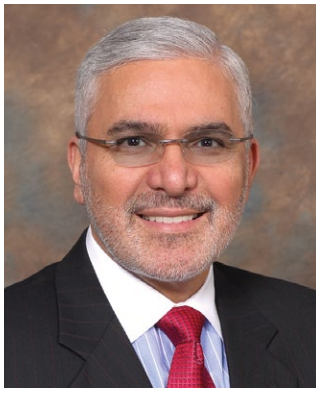

Henry A. Nasrallah, MD
Editor-in-Chief

Brain and mind assessment in psychiatry

A mountain of evidence indicates that psychosis and bipolar disorder (BD) are brain disorders with an array of thought, mood, cognition, and behavioral aberrations.

Yet the clinical assessment of those neuropsychiatric disorders predominantly is restricted to evaluating mental and behavioral signs and symptoms. It's time we comprehensively assess our psychiatric patients' brains, not just describe their minds. This is the only way we can eventually identify the roots of serious mental illness and develop accurate and effective therapeutic interventions and preventions.

Consider the following brain probes, measures, and assessments that are rarely done in patients with first-episode schizophrenia, BD, or major depression. These clinical and technological cerebral evaluation methods all are available and feasible and are being routinely exploited in neurology and other medical specialties. Not using them represents missed opportunities to advance the scientific underpinnings of psychiatric diagnosis and treatment.

Complete neurologic examination, including cranial nerves, motor functions, sensory status, reflexes (including primitive reflexes), and soft neurologic signs. Psychiatrists rarely perform such examinations, although they can easily relearn and incorporate them in their critical initial assessment of severe psychiatric episodes. Researchers have identified many neurologic findings in drug-naïve psychotic patients before they receive medications in whom adverse effects may mask or add to motor or sensory abnormalities.

Neurocognitive testing. An extensive body of literature has definitively demonstrated severe cognitive deficits across multiple domains in schizophrenia, BD, and major depression. Yet, inexplicably, few first-episode patients are assessed with a standard battery of tests for memory, attention, visuospatial skills, or executive functions in clinical practice. Cognitive deficits are a product of abnormal neural pathways and neurocognitive tests can provide tremendous insight into regional and overall brain functions and provide clues for etiopathology and a road map for rehabilitation.

Neuroimaging. Multiple sophisticated techniques to assess brain structure and function are used in research but rarely in clinical practice. These include:

Morphological MRI, which can provide exquisitely detailed anatomical information about cortical and subcortical structures. This can help identify lesions that cause mania, schizophrenia-like disorders, or depression secondary to a brain pathology. Even if no lesion is found, the pattern of atrophy, hypertrophy, ectopic gray matter, or hyperplasia can help identify subtypes of heteroge-

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neous psychotic and mood disorders, and may lead to a specific diagnosis and treatment.

Magnetic resonance spectroscopy (MRS) is essentially a living biopsy of the brain in any region, detailing the spectrum and amount of various neurochemical substances (such as glutamine, γ-aminobutyric acid, creatine, N-acetylaspartic acid, or lactate) using proton spectroscopy, high energy phosphates such as adenosine diphosphate (ADP) or adenosine triphosphate (ATP) or membrane breakdown products (such as phosphomonoester and phosphodiester) using phosphorous MRS. Researchers are gradually "mapping" the regional chemistry of the brain in health and disease, which may provide profound insights for understanding the neurobiology of serious mental disorders.

Functional MRI, which can display the underactivation or overactivation of various brain regions at rest or while experiencing severe symptoms such as hallucinations or melancholia or while performing a cognitive task. Significant insights about brain pathways can be gleaned from this test.

Diffusion tensor imaging (DTI), which can assess myelin integrity and provide critical data about white matter tract pathology and intra- and inter-hemispheric disconnectivity. Pathological myelin findings in psychotic and mood disorders already are prompting novel treatments for these disabling brain illnesses.

Cerebrospinal fluid (CSF) examination. Psychiatrists rarely perform lumbar punctures (LP) in first-episode patients, although psychotic or bipolar disorders are as severe and disabling as multiple sclerosis or meningitis, where an LP is routine. This longstanding omission is the result of the antiquated notion that CSF in psychiatric patients is not abnormal and uninformative. But the fact is that CSF in patients with psychotic or mood disorders may contain many recently discovered biomarkers that shed light on the tremendous neurochemical changes during an acute psychotic, manic, or depressive episode. So the focus in psychiatry is not simply on red blood cells, white blood cells, glucose levels, or proteins, as in a routine LP, but on the emerging biomarkers of brain pathologies that have been implicated in the psychotic and mood disorders, including:

- inflammatory signaling and biomarkers (such as cytokines, interleukins, TNF-α)
- apoptotic (such as caspase-3, Fas, ARTS) and anti-apoptotic proteins (Bcl-2)
- neurotropic (growth) factor (such as BDNF, NGF, VEGF)
- oxidative stress biomarkers (such as TBARS, TRAP, PCC, SOD, and TAOP)
- myelin byproducts (such as S100B, oligodendrocytic proteins)
- glutamate/glutamine abnormalities
- lipodomic aberrations
- metabolomic profiles
- mitochondrial deficits (such as low glutathione and GPX)
- immunoglobulins (such as IgG, IgM).

If CSF analysis is done routinely, unprecedented discoveries can be made about the nature of brain pathologies and potential diagnostic biomarkers in various subtypes of serious psychiatric disorders, leading to specific and personalized treatments.

It's time that we go beyond the current descriptive approach that includes a brief mental status exam. We must conduct a comprehensive investigation of our patients' abnormal brains, which are responsible for their anomalous minds and impaired functioning. It's time to capitalize on the amazing neuroscience advances to understand our patients' brains. It's time that we employ translational psychiatry to guide our diagnosis and treatment of severe mental disorders.

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