



Henry A. Nasrallah, MD Editor-in-Chief

Psychosis may be a secondary symptom that emerges as a consequence of cognitive impairment

Is schizophrenia a psychotic disorder?

Ask any mental health professional to give an example of a major psychotic disorder, and the most likely answer would be schizophrenia. But is schizophrenia really a psychotic disorder? And if not, then what is it, and how do you explain the psychotic symptoms associated with the disorder?

Research and clinical observation tell us that psychosis is a secondary feature of schizophrenia. This brain disease's enduring and most disabling components are cognitive deficits and negative symptoms, both of which have been shown to precede the onset of psychotic symptoms. Because the core deficit is cognition—especially short-term memory and executive functions—individuals with schizophrenia are unable to return to the classroom or hold a job even when medications have suppressed their psychotic symptoms. Impaired social cognition can:

- masquerade as negative symptoms, such as poor social skills
- result in positive symptoms, such as ideas of reference or paranoid delusions, when the individual with schizophrenia misperceives ordinary social cues as "threats."

Cognitive aberrations, including perceptual distortion, also contribute to delusions and hallucinations. Persons with schizophrenia are rarely identified as "ill" or hospitalized for acute psychiatric care until their behavior becomes bizarre with the appearance of psychotic symptoms. In fact, most practitioners do not apply the diagnostic label of schizophrenia until the individual manifests delusions, hallucinations, and bizarre behavior, and rarely—if ever—are cognitive functions assessed during initial evaluations (except in research settings). It may be that psychosis emerges as a consequence of cognitive deficits caused by adverse neurodevelopment and neurodegenerative and neurochemical changes.

Psychosis in medical disorders. Many genetically transmitted medical disorders can manifest with psychotic symptoms but are never labeled "psychotic disorders." Examples include albinism, congenital adrenal hyperplasia, erythropoietic protoporphyria, Fabry's disease, familial basal ganglia calcification, G6PD deficiency, Gaucher's disease, hemochroma-

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From the **Editor**

tosis, Huntington's chorea, hyperasparaginism, ichthyosis vulgaris, Kartagener's syndrome, Klinefelter's syndrome (karyotype 47,XXY), metachromatic leukodystrophy, Niemann-Pick disease, phenylketonuria, acute intermittent porphyria, Turner's syndrome, and Wilson's disease.

Medical disorders that include occasional psychotic symptoms may share neurobiologic features with schizophrenia and could provide clues about the neural pathways that generate delusions or hallucinations. But few of these disorders share schizophrenia's core features of adverse neuroplastic changes and clusters of cognitive dysfunction and negative symptoms.

Targeting cognitive dysfunction in schizophrenia.

Researchers are seeking ways to improve short-term memory and executive function in persons with schizophrenia, whose scores on these cognitive measures fall 1 to 3 standard deviations below the average of the general population. The National Institute of Mental Health, for example, has funded the MATRICS initiative (Measurement and Treatment Research to Improve Cognition in Schizophrenia). Several candidate drugs that may serve as possible "cognitive enhancers" are being tested—for use in combination with antipsychotics—to help individuals with schizophrenia function better in social and employment settings.

Will negative symptoms—and even some positive symptoms—be ameliorated when cognition is improved? We'll have to wait and see.

Perhaps DSM-V—planned to appear around 2012 should reconceptualize schizophrenia as a neurodevelopmental/neurodegenerative disorder characterized by a deficit syndrome and cognitive dysfunction, with intermittent secondary psychotic episodes. Or maybe we can go back to Kraepelin's prescient nomenclature: dementia praecox!

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