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EDITORIAL

Boundaries of the Psychosis Phenotype

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Since Emil Kraepelin classified psychosis into 3 major categories (organic, affective, and schizophrenic) in the late 19th century, the unitary concept of psychosis was abandoned. This categorical conceptualization of psychosis was more or less accepted by clinicians through the 20th century with some refinements. During my residency training, teachers would highlight qualitative differences in reality distortions across disorders; for instance, unusual visual perceptual distortions associated with substance abuse or the affective tone of delusional thinking in psychosis associated with bipolar illness. Such observations were used to support the categorical view of psychosis and stress phenomenological and biological differences in psychosis across various major psychotic disorders.

In the past several years, extensive epidemiological and clinical research has yielded information that challenges the categorical models of psychosis. Epidemiological studies of self-reported psychotic symptoms of hallucinations and delusions show that about a quarter of the general population endorse such symptoms. Multivariate taxometric analyses of these epidemiological survey data suggest a dimensional rather than taxonomic structure for these psychotic experiences.[1] Within this dimensional model of psychosis, symptoms vary in severity with most persistent and severe psychosis needing treatment (see Jim van Os and Richard Linscott in the current issue[2]). There is no discontinuity of psychosis across major psychotic disorders such as schizophrenia and bipolar disorders, although the frequency of symptoms and severity may vary. Less severe symptoms may indicate vulnerability to develop schizophrenia or bipolar disorder or even the prodromal phase particularly in individuals with a family history of these disorders. The dimensional model further posits that the underlying biological underpinnings are uniform. This thesis is supported by neurocognitive and neurophysiological findings in individuals with schizotypal personality disorders, with magical thinking, perceptual distortions, and rare hallucinations indicating the lower end of the psychosis dimension. Furthermore, the dimensional model would suggest that psychotic symptoms occurring in different psychiatric disorders such schizophrenia and bipolar disorder share the same neurobiology and etiological factors.

The hypothesis of an extensive overlap in the phenomenology and etiopathophysiology of psychosis occurring across different disorders is a fundamental challenge to the Kraepelinian conceptualization of major psychotic disorders. Several lines of evidence support this hypothesis: phenomenological similarities in psychosis across disorders are frequently observed in clinical practice. Slight qualitative differences in reality distortions can easily be due to the modulating effects of the other features of the disorder. For instance, depressed or elated mood may modulate the expression of psychotic symptoms in affective illness. Studies have extensively compared brain function and structure in order to define the underlying neurobiology of psychosis in different conditions. Findings suggest a large overlap in cognitive impairments in schizophrenia and psychotic affective disorders.[3] Similarly, sensory gating, sensory-motor gating, eye tracking, and other information processing impairments known to mark schizophrenia liability are frequently observed in other psychotic disorders.[4] Brain imaging studies show some overlap but there are significant differences brain structure between schizophrenia and bipolar disorder.[5] Most of these findings come from studies in patient cohorts that support the notion of shared neurobiology, but very few studies compare neurobiology among nonill relatives of psychotic disorders. Similar neurobiological findings in relatives of probands with different psychotic disorders would implicate shared etiological, likely genetic, factors. The Bipolar and Schizophrenia Network on Intermediate Phenotypes (B-SNIP) was organized specifically to address this issue. The consortium has recruited about

a thousand families of schizophrenia and bipolar disorder with psychosis probands and administered a comprehensive battery that includes cognitive, neurophysiological, and brain imaging measures. Findings from this project will clarify the extent of overlap in the etiopathophysiology of psychosis in schizophrenia and bipolar disorders. Previous genetic studies have identified several linkage "hot-spots" (such as 18p11, 22q11, 13q32, 10p14, and 1q32) and candidate genes (such as *DISC1, NRG1, Dysbindin, NOS1, GRM4*, and *G30*/*G72*) that are implicated both in schizophrenia and bipolar disorder.[6]

Together, these data suggest psychotic symptoms that occur in different conditions are in most part similar in phenomenology, neurobiology, and etiology. However, studies have also found significant differences in brain function and structure between schizophrenia and bipolar disorder cohorts. These findings may be driven by unique aspects of each of these disorders. For instance, neurobiology associated with the affective component of the bipolar disorder, or the primary negative symptoms in schizophrenia, may explain the differences found in neurobiology between the 2 disorders. Studies similar to the B-SNIP project that also include families of probands with nonpsychotic bipolar and schizoid disorders are needed to clarify to what extent the neurobiology of psychosis is uniform across disorders.

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