Does Biology Transcend the Symptom-based Boundaries of Psychosis?

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KEYWORDS

• Psychosis • Biotype • Neurobiology • Reclassification • Schizophrenia • Schizoaffective • Bipolar

KEY POINTS

- Psychotic disorders overlap considerably in terms of clinical symptoms, familial patterns, risk genes, and treatment response.
- Numerous neurobiological measurements also fail to distinguish the most prevalent classic psychotic disorders (schizophrenia, schizoaffective, and psychotic bipolar) from each other.
- Statistical methods applied to such biological measurements in large numbers of these patients result in novel classifications that cut across traditional diagnostic boundaries, to reveal "Biotypes": biologically defined entities.
- Such new types of classification approaches within psychotic illnesses hopefully represent an opportunity to move away from phenomenologically defined syndromes in psychiatry and toward neurobiologically defined diseases.

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INTRODUCTION

Most clinical psychiatrists are undoubtedly confident in their ability to diagnose patients with schizophrenia correctly, and to distinguish them straightforwardly from individuals with other disorders manifesting similar symptoms. In so doing, they would likely mention *Diagnostic and Statistical Manual of Mental Disorders* (DSM) criteria, say something about a presumed unique underlying neurobiology, and invoke the name of Emil Kraepelin as having settled these distinctions more than a century ago. Because questioning our assumptions is always a useful exercise, this initial article is designed both to accomplish that aim by challenging these assumptions, as well as to provide a general conceptual lens through which some of the other articles in this issue can be viewed.

AN HISTORICAL PERSPECTIVE

Given that much of our current clinical classification within psychosis begins with Kraepelin, it is appropriate to start with a brief discussion of the great diagnostic divide that he promulgated in the late nineteenth century, a delineation that survives and is seldom challenged by clinicians today. Kraepelin made a fundamental diagnostic distinction within serious mental illnesses between those conditions that are clearly recurrent and episodic with between-episode recovery ("manic-depressive insanity") and another syndrome characterized by lack of recovery plus longitudinal deterioration of personality and intellect ("dementia precox"),[1] subsequently termed "schizophrenia" by Bleuler.[2] Most aspects of this classification are still present in our diagnostic manuals, although Kraepelin's schema has been altered in subtle ways over time.[3] For example, major depressive disorder, because it was recurrent, was certainly included within his purview of manic-depressive insanity; single episodes of mania, because they were not repeated, were not within the definition.[3] Kraepelin provided many detailed case examples of manic-depressive insanity in which patients clearly manifested psychotic symptoms, so that hallucinations, formal thought disorder, and delusions, the defining symptoms of psychosis, were certainly not limited to cases of schizophrenia; the predominant emphasis was on longitudinal course rather than cross-sectional symptoms. Although (as we will soon discuss) there are troubling problems and inconsistencies with Kraepelin's delineation, it has persisted for more than 100 years because no better diagnostic categorization system arose to replace it.

PROBLEMS WITH KRAEPELIN'S DISTINCTION

First, within much of clinical medicine there are obvious diagnostic boundaries, or "points of rarity" between distinct disorders. However, for schizophrenia and bipolar disorder, there are often areas of symptomatic overlap and substantial numbers of patients are not prototypical, with many left in a diagnostic muddle. This is due both to heterogeneity within these diagnoses and overlap between them, or as has been said, "patients don't read DSM." For example, in the realm of long-term outcome, some patients with otherwise typical bipolar disorder have clearly progressive chronic courses,[4] whereas it was recognized early that some patients with otherwise clinically typical schizophrenia show solid clinical recovery[5] and/or manifest prominent affective symptoms. These and other observations led Kasanin to propose a third diagnostic entity of "schizoaffective disorder" in 1933,[6] that many clinicians believe has served only to complicate issues, is a diagnostic evasion, and was necessitated only by a lack of clear diagnostic demarcation between many cases of schizophrenia and bipolar illness. Similar findings have been demonstrated recently.[7]