In a few weeks, the American Psychiatric Association will release its new edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5). This volume will tweak several current diagnostic categories, from autism spectrum disorders to mood disorders. While many of these changes have been contentious, the final product involves mostly modest alterations of the previous edition, based on new insights emerging from research since 1990 when DSM-IV was published. Sometimes this research recommended new categories (e.g., mood dysregulation disorder) or that previous categories could be dropped (e.g., Asperger’s syndrome).¹

The goal of this new manual, as with all previous editions, is to provide a common language for describing psychopathology. While DSM has been described as a “Bible” for the field, it is, at best, a dictionary, creating a set of labels and defining each. The strength of each of the editions of DSM has been “reliability” – each edition has ensured that clinicians use the same terms in the same ways. The weakness is its lack of validity. Unlike our definitions of ischemic heart disease, lymphoma, or AIDS, the DSM diagnoses are based on a consensus about clusters of clinical symptoms, not any objective laboratory measure. In the rest of medicine, this would be equivalent to creating diagnostic systems based on the nature of chest pain or the quality of fever. Indeed, symptom-based diagnosis, once common in other areas of medicine, has been largely abandoned.

Patients with mental disorders deserve better. NIMH has launched the Research Domain Criteria (RDoC) project to transform diagnosis by incorporating genetics, imaging, cognitive science, and other levels of information to lay the foundation for a new classification system. Through a series of workshops over the past 18 months, we have tried to define several major categories for a new nosology (see below). This approach began with several assumptions:

- A diagnostic approach based on the biology as well as the symptoms must not be constrained by the current DSM categories,
- Mental disorders are biological disorders involving brain circuits that implicate specific domains of cognition, emotion, or behavior,
- Each level of analysis needs to be understood across a dimension of function,
- Mapping the cognitive, circuit, and genetic aspects of mental disorders will yield new and better targets for treatment.

It became immediately clear that we cannot design a system based on biomarkers or cognitive performance because we lack the data. In this sense, RDoC is a framework for collecting the data needed for a new nosology. But it is critical to realize that we cannot succeed if we use DSM categories as the “gold standard.”

The diagnostic system has to be based on the emerging research data, not on the current symptom-based categories. Imagine deciding that EKGs were not useful because many patients with chest pain did not have EKG changes. That is what we have been doing for decades when we reject a biomarker because it does not detect a DSM category. We need to begin collecting the genetic, imaging, physiologic, and cognitive data to see how all the data – not just the symptoms – cluster and how these clusters relate to treatment response.

That is why NIMH will be re-orienting its research away from DSM categories. Going forward, we will be supporting research projects that look across current categories – or sub-divide current categories – to begin to develop a better system. What does this mean for applicants? Clinical trials might study all patients in a mood clinic rather than those meeting strict major depressive disorder criteria. Studies of biomarkers for “depression” might begin by looking across many disorders with anhedonia or emotional appraisal bias or psychomotor retardation to understand the circuitry underlying these symptoms. What does this mean for patients? We are committed to new and better treatments, but we feel this will only happen by developing a more precise diagnostic system. The best reason to develop RDoC is to seek better outcomes.

RDoC, for now, is a research framework, not a clinical tool. This is
a decade-long project that is just beginning. Many NIMH researchers, already stressed by budget cuts and tough competition for research funding, will not welcome this change. Some will see RDoC as an academic exercise divorced from clinical practice. But patients and families should welcome this change as a first step towards "precision medicine," the movement that has transformed cancer diagnosis and treatment. RDoC is nothing less than a plan to transform clinical practice by bringing a new generation of research to inform how we diagnose and treat mental disorders. As two eminent psychiatric geneticists recently concluded, “At the end of the 19th century, it was logical to use a simple diagnostic approach that offered reasonable prognostic validity. At the beginning of the 21st century, we must set our sights higher.”

The major RDoC research domains:

- Negative Valence Systems
- Positive Valence Systems
- Cognitive Systems
- Systems for Social Processes
- Arousal/Modulatory Systems

References


