

Letter to Editor

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Letter

Diagnostic categories in psychiatry like Diagnostic and Statistical Manual (DSM) and International Classification of Diseases (ICD), based upon presenting signs and symptoms, fail to align with findings emerging from clinical neuroscience and genetics. One consequence has been to slow the development of new treatments targeted to underlying pathophysiological mechanisms. The National Institute of Mental Health (NIMH) is launching the Research Domain Criteria (RDoC) project to create a framework for research on pathophysiology, especially for genomics and neuroscience, which ultimately will inform future classification schemes ensuring diagnosis that has both reliability and validity. Identifying syndromes based on pathophysiology will eventually be able to improve outcomes. Incorporating data on pathophysiology in ways that eventually will help identify new targets for treatment development, detect subgroups for treatment selection, and provide a better match between research findings and clinical decision making.

RDoC classification rests on three assumptions. First, the RDoC framework conceptualizes mental illness as brain disorders. In contrast to neurological disorders with identifiable lesions, mental disorders can be addressed as disorders of brain circuits. Second, RDoC classification assumes that the dysfunction in neural circuits can be identified with the tools of clinical neuroscience, including electrophysiology, functional neuroimaging, and new methods for quantifying connections *in vivo*. Third, the RDoC framework assumes that data from genetics and clinical neuroscience will yield bio-signatures that will augment clinical symptoms and signs for clinical management. Examples where clinically relevant models of circuitry-behavior relationships augur

future clinical use include fear/extinction, reward, executive function, and impulse control. For example, the practitioner of the future could supplement a clinical evaluation of what we now call an “anxiety disorder” with data from functional or structural imaging, genomic sequencing, and laboratory-based evaluations of fear conditioning and extinction to determine prognosis and appropriate treatment, analogous to what is done routinely today in many other areas of medicine.

NIMH views RDoC as the beginning of a transformative effort that needs to succeed over the next decade and beyond to implement neuroscience-based psychiatric classification. Just two weeks before DSM-5 is due to appear, Thomas R. Insel, M.D., Director of the NIMH, made clear the agency would no longer fund research projects that rely exclusively on DSM criteria. Henceforth, the NIMH, which had thrown its weight and funding behind earlier editions of the manual, would be “re-orienting its re-search away from DSM categories.” “The weakness of the manual”, he explained “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”.

RDoC is intended as a framework to guide classification of patients for research studies, not as an immediately useful clinical tool. While the hope is that a new way forward for clinical diagnosis will emerge sooner rather than later, the initial steps must be to build a sufficient research foundation that can eventually inform the best approaches for clinical diagnosis and treatment. It is hoped that by creating a framework that interfaces directly with genomics, neuroscience, and behavioral science, progress in explicating etiology and suggesting new treatments will be markedly facilitated.

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