

NEWS

Funding agency seeks to dismantle diagnostic barriers

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In 2010, National Institute of Mental Health (NIMH) director **Thomas Insel** proposed an overhaul in the way scientists think about conditions that affect the mind and brain: Instead of putting people into diagnostic boxes — autism, say, or schizophrenia — based on their symptoms, Insel lobbied for a classification system, called **Research Domain Criteria (RDoC)**, with a strong foundation in biology.

In September, Insel **announced** his departure from the NIMH for a job with the life sciences team at Google, raising questions about RDoC's future. But the agency's new leaders say they plan to forge ahead with the program.

"We don't see RDoC as being wedded to any one person. It's a priority within NIMH," says **Sarah Morris**, acting director of the RDoC unit.

Insel sought to transform mental health research by moving away from traditional, behavior-based diagnoses. Current diagnostic categories, such as those outlined in the "Diagnostic and Statistical Manual of Mental Disorders" (**DSM-5**), don't map neatly onto findings about brain circuits and genetic variants, he wrote in a February 2010 **blog post**. And effective treatments for brain disorders remain elusive.

To lay the groundwork for a new diagnostic rubric, Insel introduced a set of guidelines that encourage researchers to explore mental health through the lens of psychology and neuroscience. These criteria focus on parsing traits and abilities, such as fear and memory, to trace biological and genetic paths to mental illness.

Insel put financial firepower behind his strategy in April 2013, when he announced that the NIMH would **shy away from funding proposals** based on diagnostic categories in favor of projects rooted in RDoC principles.

The agency plans to continue to back projects based on RDoC guidelines, and researchers are pooling data from these studies in a database, says Morris.

The autism community has mixed feelings about RDoC. Many researchers agree that symptom-based diagnoses need more biological backing, but others say that reducing complex behaviors to specific circuits and genetic mutations misses the forest for the trees.

“Ultimately, what we want to change is behavior,” says **Catherine Lord**, director of the Center for Autism and the Developing Brain in New York City.

Boundary breakdown:

Conceptions of mental illness shift over time, a history painstakingly chronicled in the DSM, the U.S. diagnostic bible that is revised periodically. The DSM diagnoses provide a common reference point for doctors as well as researchers, so that one study’s reference to ‘autism’ is consistent with another’s.

But the boundaries between mental disorders are often messy. Symptoms common to more than one condition blur these lines, and individual differences in the expression of certain behaviors obscure the areas in between, experts say.

“Brain disorders and other chronic medical disorders that physicians deal with are multifactorial and won’t settle neatly into categories,” says **Eric London**, director of the Autism Treatment Research Laboratory at the New York State Institute for Basic Research in Developmental Disabilities.

The RDoC framework is an initial attempt to address this imperfect fit. It shifts the focus from the more than 100 diagnostic boxes in the DSM-5 to five dimensions of thought and behavior: cognition, social processes, arousal, and responses to aversive and rewarding situations. Researchers can explore parts of a dimension — for example, looking into working memory or language within ‘cognition’ — as they relate to mental health.

The idea is for researchers to use various techniques, such as brain imaging and genetic analyses, to identify neural circuits and **biomarkers** underlying these dimensions. The approach may ultimately serve as a stepping stone to treatments tailored to specific groups or individuals.

The criteria also break diagnostic barriers by encouraging researchers to study the full range of behavior, rather than labeling it as ‘normal’ or ‘abnormal.’ Looking at behavior on a continuum may provide a richer understanding of mental illness, Morris says. “We miss out on important information if we only study individuals with diagnosable disorders.”

London says he would like to see RDoC extended to the clinic. In a 2014 editorial, he called for

doctors to keep in-depth medical records that **detail a person's every symptom** instead of simply naming a diagnostic category¹. This approach could inform research by identifying patterns of symptoms across individuals.

Category controversy:

The criteria are still in their infancy, and implementing them is likely to be an incremental, dynamic process, Morris says. For instance, researchers still have to identify the optimal areas to explore within each domain, as well as the best ways to explore them.

They also have to figure out how to balance the goals of RDoC with the behavioral focus of other diagnostic systems, such as the DSM. If they don't, some experts say the emphasis on brain circuits and animal models threatens to relegate behavior to the sidelines.

"It's a well-intentioned goal to link biology to behavior; the bad thing is that it demotes behavior to this minor thing," says Lord, who helped to craft the DSM-5.

Many proponents of RDoC advocate for a hybrid approach in which researchers investigate RDoC domains within DSM-defined conditions. For example, scientists could break the diagnosis of 'autism' into subtypes according to certain behavioral or cognitive traits. Some research already suggests that individuals with autism fall into different categories based on their symptoms and patterns of gene expression².

"RDoC and the DSM are not mutually exclusive," says **Bruce Cuthbert**, acting director of the NIMH, who led the RDoC unit until Insel left the institute in November.

Even so, making progress will require a major shift in mindset. Diverging from the long-held silos of traditional diagnoses is likely to take more than just a few decades, London says. "This is probably close to an infinite process."

REFERENCES:

1. London E.B. *Trends Neurosci.* **37**, 683-686 (2014) [PubMed](#)
2. Hu V.W. *Autism Res.* **2**, 78-97 (2009) [PubMed](#)