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Research Domain Criteria -- RDoC

By Thomas Insel on March 06, 2012

While basing diagnosis exclusively on signs and symptoms was typical of mid-twentieth century medicine, by the beginning of the twenty-first century, most disciplines had built many other sources of information, such as biomarkers, into their diagnostic toolkits. Imagine diagnosing heart attack only by characterizing chest pain or using the symptoms of fever to distinguish bacterial from viral pneumonia. A recent report from the National Academy of Sciences, *Towards Precision Medicine (see my previous blog on improving diagnosis through precision medicine*), described how improving diagnostic specificity for cancer has transformed outcomes by identifying the precise biology of each patient's tumor and linking this diagnosis to targeted treatments.

In contrast to these changes in the rest of medicine, for the past century mental disorders have been considered "behavioral," implying that an exclusive focus on symptoms could yield a precise diagnosis. Problems with this narrow approach to diagnosis began to emerge as research demonstrated the inescapable heterogeneity underlying diagnostic labels such as depression or schizophrenia. Even attempts to subdivide these categories by considering additional symptoms, such as anxious depression, failed to give reliably better prediction of treatment response. Recent research in genetics and brain imaging suggest that biological measures may help us to understand the heterogeneity within the symptoms of mental illness. Just as with chest pain and fever, by adding more tools to our diagnostic toolkit, current labels such as "depression" or "schizophrenia" might give way to more precise categories. These advances have the potential to revolutionize the way we classify and, importantly, treat mental disorders.

Last week, NIMH hosted the latest in a series of workshops to launch the Research Domain Criteria (RDoC) project. RDoC is an experimental approach to the classification of mental disorders that incorporates multiple dimensions: behavior, thought patterns, neurobiological measures, and genetics. The immediate aim of the project is not to develop a diagnostic system for clinicians or patients. While I expect RDoC will ultimately transform practice, the near-term goal is to provide a framework for research. For instance, the meeting this week focused on social processes, reviewing what we know and what we need to understand about the deficits in social cognition and social behavior in what we now call autism, schizophrenia, depression, and anxiety disorders in both adults and children. The underlying assumption is that approaching mental disorders along this dimension may yield a more precise, more individualized diagnosis that crosses our current labels. But this is not simply about finding links between the social deficits of people with autism and people with social anxiety. RDoC uses genetics, imaging, and cognitive science for understanding deficits in social behavior.

This is not as simple as it sounds. Genes identified as conveying risk for mental illness don't track neatly with any of the currently recognized disorders. Nearly all of the genes associated with risk for schizophrenia also contribute to risk for bipolar disorder and autism. One could use this information to dismiss genetics as "non-specific." But certainly it is more parsimonious to conclude that nature does not define the disorders designated by our current diagnostic labels, all of which were devised by committees of clinicians who were voting on the symptoms. While the impact of individual genes on risk is likely to be small and not specific to any existing current diagnostic category, could genetics be showing us a different way to map the diagnostic landscape?

The RDoC project has a primary focus on neural circuits. Accumulating findings on the neural circuitry that generates behavior is making it possible to envision such an approach. While genes cut across the current diagnostic labels, neuroimaging often helps us to sub-divide current groups. By studying patterns of brain activity either at rest or with activation, we can begin to let the brain tell us the different forms of mood, anxiety, or psychotic disorders. Of course, this is exactly the approach to diagnosis in neurology, where imaging is used routinely for localizing lesions, rather than relying exclusively on motor or sensory changes.

Still being developed, the RDoC system began with five broad domains of psychological function that appear especially ripe for integration with recent developments in neuroscience. In addition to social processes, these are cognitive systems (attention, perception, working memory), positive valence systems (reward, appetitive behaviors), negative valence systems (depression, defeat, loss), and arousal-regulatory systems (activity, sleep, rhythms). These domains cut across diagnostic categories; as a result, the organization emerging from RDoC is unlikely to parallel existing diagnostic categories. In contrast to current systems where a disorder is either present or absent, the RDoC approach to psychopathology is dimensional; that is, it incorporates measures of magnitude or severity, analogous to tests of blood pressure or cholesterol. One of the important aspects of the RDoC project will be to develop readily administered tests to provide this kind of dimensional information in reliable and valid ways.

The Institute recently solicited applications for funding research projects aimed at testing and validating functional relationships identified in RDoC. By 2013, RDoC-themed projects will represent an increasing share of the Institute's clinical research. Indeed, we plan to use RDoC as a framework for guiding our funding, leading to a new nosology for mental disorders.

Much remains to be learned about the complexities of how the brain implements psychological functions. It is hoped that in the future, a classification system in the mold of RDoC will bring our approach to mental illness closer to a vision of precision medicine in which a diagnosis pinpoints, to the extent possible, dysfunction specific to an individual and treatment is targeted accordingly.

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Posts by Topic

Disorders

- Attention Deficit Hyperactivity Disorder (ADHD) (3 Items)
- Autism (15 Items)
- Bipolar Disorder (4 Items)
- Borderline Personality Disorder (1 Item)
- Depression (6 Items)
- Eating Disorders (1 Item)
- Obsessive-Compulsive Disorder (OCD) (2 Items)
- Post-Traumatic Stress Disorder (6 Items)
- Schizophrenia (13 Items)

Populations

- Military Servicemembers (2 Items)
- Women's Mental Health (1 Item)
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Research

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Other

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- Diversity and Ethnic Groups (5 Items)
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