Editorial

The Research Domain Criteria: moving the goalposts to change the game

Joanne L. Doherty and Michael J. Owen

Summary

There is increasing concern that a reliance on the descriptive, syndrome-based diagnostic criteria of ICD and DSM is impeding progress in research. The USA's major funder of psychiatric research, the National Institute of Mental Health (NIMH), have stated their intention to encourage more research across diagnostic categories using a novel framework based on findings in neuroscience.

Declaration of interest

None.

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Problems with current classifications

Our current diagnostic criteria have many shortcomings; comorbidity is common, there is considerable heterogeneity within categories and no clear boundaries exist between illness and health. However, there is general agreement that we lack, by some distance, a scientific rationale for a major overhaul, and the current DSM and ICD schemes, albeit with occasional tinkering, seem set to remain the cornerstone of clinical practice for some time. In contrast, there are good reasons for being concerned that the almost exclusive use of traditional diagnostic categories in research is impeding progress.[1,2] This has been fuelled by a realisation that many risk factors, whether genetic or environmental,[3] and neural circuit abnormalities[4] appear to operate across diagnoses. It is hard to avoid the conclusion that, if research continues to group patients largely on the basis of descriptive categories that do not appear to map onto underlying mechanisms, we will continue to struggle to understand pathogenesis or develop novel diagnostic tests.[2,5]

The need for a new approach

Although many agree that a new, more valid, approach is needed, it remains virtually mandatory to use either DSM or ICD criteria in research grants and papers. However, this seems set to change since Thomas Insel, Director of the National Institute of Mental Health (NIMH), announced the following on his blog in April 2013: '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 subdivide current categories – to begin to develop a better system'.[6] The vehicle of this transformation will be the Research Domain Criteria (RDoC) project whose aim is to 'transform diagnosis by incorporating genetics, imaging, cognitive science and other levels of information to lay the foundation for a new classification system'.[6] The timing of this announcement just a few weeks before the release of DSM-5 ensured that it received maximum publicity, and it was widely seen as an attack on the diagnostic practices that underpin patient care and an edict that NIMH would no longer fund research using DSM criteria.

The RDoC project

The NIMH has been developing the RDoC project since 2009.[7] The RDoC is essentially a framework to guide research and to relate research findings across levels of organisation. An explicit goal is to lay the foundations for a new psychiatric classification system. The central organising principle is that mental disorders are best viewed as biological and psychological disorders involving brain circuits. The project aims to define the basic dimensions of dysfunction that cut across disorders as traditionally categorised, in order to develop new ways of classifying psychopathology based on domains of observable behaviour and their relationship to markers of potential underlying causes and mechanisms.

The RDoC is a dimensional system, which spans the range from normal to abnormal. It is conceptualised as a matrix with four dimensions: (a) domains of functioning, which are further subdivided into dimensional constructs; (b) units of analysis; (c) developmental aspects (changes to the constructs over time); and (d) environmental aspects (how the environment affects and interacts with the constructs). The development of the matrix is a dynamic process and modifications to its structure and content will be made as more evidence accumulates.

The rows and columns of the matrix correspond to domains of functioning and units of analysis respectively; with developmental and environmental aspects acting orthogonally. The domains of functioning and the dimensional constructs contained within them have been selected based on current understanding of neural circuitry. That is, whether there is evidence implicating particular brain circuits in that dimension or domain. The domains that are currently represented in the matrix are: negative valence systems; positive valence systems; cognitive systems; systems for social processes; and arousal/regulatory systems. Units of analysis are the different classes of variable that can be used to study the domains and constructs. These are genes, molecules, cells, circuits, physiology, behaviour and self-reports.[8]

Investigators employing the RDoC approach will typically select a dimensional construct from the five domains of functioning. The construct will then be studied using one or more units of analysis. For example, it is known that chromosomal abnormalities known as copy number variants (CNVs) confer risk of psychopathology and cognitive impairment. To better understand the effects of a particular CNV on cognitive systems patients could

be recruited from a clinical genetics service. Patients who carry the CNV of interest could then be compared with non-carriers on a dimension of cognition, such as attention. In this example, CNV status would be the independent variable and the dependent variables would be performance during tasks of attention. The units of analysis employed by this study would therefore be genes and behaviour.

Implications

Some of the alarm that followed Insel's blog posting has been dissipated by subsequent clarification that NIMH supports DSM-5 and ICD-10 as 'the contemporary consensus standard for how mental disorders are diagnosed and treated'.[9] Further clarification was aimed at reassuring researchers that NIMH will not stop funding research based on DSM. Rather, there will be a 'shift in emphasis' so that researchers will be encouraged to work across current criteria and no longer be required to frame studies within the constraints of DSM.[10] This is critical because if NIMH impose rigid and sole adherence to RDoC, progress could be impeded in the same manner as the recent rigid adherence to ICD and DSM. However, these clarifications leave one uncertain as to the likely extent of RDoC's implementation and the speed with which the change in emphasis will occur. What does seem clear is that this policy can only succeed if there is buy-in from the US research community, who not only submit grants but who also play a significant role in peer review of research grant applications.

Some potential issues arise in considering different aspects of the RDoC project. The first set of concerns relate to whether particular research areas will be disadvantaged. For example, the focus on domains and constructs with identified neurobiological underpinnings runs the risk of diverting funding away from certain types of psychopathology. The counter argument might be that identification of gaps such as these should stimulate research on the associated neuroscience and NIMH would see this as refining the RDoC process. Perhaps of more concern is that RDoC's focus on neural circuits might undermine research on psychological processes and mechanisms. It is to be hoped that as the project develops psychological mechanisms will become more explicitly represented within the framework. Other research areas for which the RDoC approach might pose challenges are those such as epidemiology and genomics where very large population samples are required to implicate novel risk factors. If we are really serious about leveraging the power of unbiased genomic and phenomic approaches to identify novel risk factors that have an impact on specific aspects of brain structure and function that underlie mental illness, then we are going to need to assemble very large and deeply phenotyped cohorts. This will require greater collaboration and data sharing between neuroscientists and a strong focus on large sample sizes and robust levels of statistical significance. There is nothing in the nature or specifications of the RDoC project that would preclude these kinds of large-scale studies, and in fact such projects might be ideal for relating genetics to various other measures with respect to RDoC constructs. However, some measures, in particular neuroimaging measures such as functional magnetic resonance imaging, will be difficult to apply to samples of thousands. Having said this, other behavioural, cognitive, symptom or electrophysiological measures might well be sufficiently scalable. Moreover, one explicit subgoal of RDoC is to foster new methods of measurement, and these might indeed be tailored to the goal of feasible deeply phenotyped cohorts.

The RDoC framework is not intended for use as a diagnostic tool; ICD and DSM will remain central to clinical practice until the neuroscientific advances facilitated by RDoC can be translated into the clinical setting. There is some concern that the disparity between RDoC and clinical diagnostic practice could create a gulf between academic and clinical psychiatry. Close collaboration between academic and clinical psychiatrists will therefore be crucial to the successful development of the project and its clinical translation. It is reassuring that NIMH are apparently actively assessing how communication across the two systems can be facilitated.[10]

An area that perhaps requires more consideration is the possibility that variation in the course and outcome of psychiatric disorders indexes differences in underlying pathogenesis. The need to take developmental variables into account is recognised but there is also a pressing need to bring advances in genetics, imaging and cognitive science together with detailed longitudinal clinical studies across the lifespan.

Finally, some are concerned that by admitting the inadequacies of our diagnostic categories we are undermining the practice of psychiatry and giving ammunition to its detractors. We believe that psychiatry's acknowledgment of its diagnostic shortcomings is a sign of its maturity. Psychiatric disorders are the most complex in medicine and some of the most disabling. We have treatments that help some of the people some of the time, but we need to develop new treatments and new ways of targeting treatments to those who will best respond.

Conclusions

The RDoC project is a bold and radical response to the short-comings of current classifications for research. However, it is a long-term undertaking and it will take a decade or more before we can expect transformational findings. We are reassured that it will continue to be rolled out as part of a mixed economy, targeted at the most tractable questions, and that it has the potential to be developed and refined as new research findings accumulate. It is clear that if research is to yield the improvements in diagnosis and treatment heralded by rapid developments in genetics and neuroscience, a new and systematic approach to study mental disorder is needed. The RDoC project is the first large-scale effort to research mental disorders in a bottom-up, neural-circuit-led manner and has the potential to transform psychiatry and improve the lives of our patients.

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psychiatry in pictures

Pool of Tears

P.H.

I was born [on] 20 March 1943 and have lived in East Devon since 1994. I began to create fantasy drawings around 1968. I lived in a dream world, but when life hit me hard in 1973, I fell ill and suffered a major breakdown. Since then, gradually over many years, I have tried to live for the day and in the real world, which has proved very difficult for me. I didn't discover I had schizophrenia until the early 1980s and was unaware I had suffered with the illness since my teens. 'Pool of Tears' was created in 1972, before my collapse. My creative output was great at this time and the picture expresses how I felt then. Originals poured out of me – I couldn't stop drawing and inspiration came easily to me. The girl is trapped and crying – hence 'Pool of Tears' – while the small figure [in the background] has broken free and is dancing.

I was trying desperately to escape my environment and leave suburbia for a life of my own. I had relationship problems and couldn't cope, so 'I fell from Grace like rotting lace', a line from one of my many poems expressing how I feel. Now I have become more mature. I try to live in Reality.

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