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Misunderstanding RDoC

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Abstract

Mental illness is fundamentally mental, by definition about psychological rather than biological phenomena, but biological phenomena play key roles in understanding, preventing, and treating mental illness. The Research Domain Criteria initiative (RDoC) of the US National Institute of Mental Health is an unusually ambitious effort to foster integration of psychological and biological science in the service of psychopathology research. Some key features and common misunderstandings of RDoC are discussed here.

Keywords

RDoC; categorical diagnosis; dimensional diagnosis; reductionism; endophenotype

Sometimes as a new concept or initiative begins to gain traction, it comes to be misunderstood in consistent ways. Such concerns can propagate, so that problems to which the new initiative is not vulnerable are seen by many as inherent in it. In the case of the Research Domain Criteria initiative (RDoC) of the US National Institute of Mental Health (NIMH; Insel et al., 2010; Kozak & Cuthbert, 2016; Sanislow et al., 2010), some such misunderstandings reflect longstanding problems in the field, problems that some assume characterize the new initiative even though the initiative was intentionally developed to solve or avoid those very problems. Correction of such misunderstandings can foster the advancement, improvement, and impact of the initiative.

RDoC has reached a stage where it is much more widely cited than understood (c.f. Iacono, 2016; Lilienfeld, 2014; Miller, Rockstroh, Hamilton, & Yee, 2016; Weinberger, Glick, & Klein, 2015; Yee, Javitt, & Miller, 2015). It is still early days for judging the full import of RDoC, but it is already clear that its impact will be profound. RDoC subsumes and goes well beyond translational research. Philosophically, it is remarkably ambitious, in a way that large institutions rarely undertake. First, RDoC proposes to get out from under the simplistic nature/nurture dichotomy that has strangled research on mental illness for decades. It is now clear that the hyperbiological approach that NIMH had adopted by 1990, at the beginning of the “Decade of the Brain” endorsed by the U.S. Congress, was mistaken in its foundation on eliminative reductionism (Lilienfeld, 2007; Miller, 1996, 2010). In particular, at the time it was widely believed that the psychological phenomena that define mental illness would eventually be fully reduced, in a philosophical sense, to biological phenomena. That is,

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psychological concepts and phenomena would eventually be replaced with biological concepts and phenomena, with psychological accounts of behavior no longer needed. Although biological phenonema are critical implementations of the psychological phenomena of mental illness, they cannot explain psychological phenomena per se (Miller, 2010). RDoC wisely puts psychology and biology back on equal footing (Kozak, 2016; Kozak & Cuthbert, 2016).

The second major philosophical ambition of RDoC is that it goes beyond merely declaring that psychology and biology must both be accounted for in theorizing about mental illness. RDoC advocates development of new, hybrid concepts that bring together important facets of what have often been thought of as (wholly separate) psychological and biological phenomena. This conceptual ambition goes beyond what we are currently capable of. The RDoC analysis of the state of the art is that decades of research (and billions of federal and corporate dollars) have produced a remarkably meager yield in the understanding, prevention, and treatment of mental illness (briefly summarized by Yee et al., 2015). The confident focus for several decades on the hunt for simple genetic mechanisms has been particularly unsuccessful in finding “the gene for” any of the major forms of mental illness. We are gradually coming to realize why that effort was doomed to failure (Kendler, 2005). Genes surely play critical roles in mental illness, but these genetic roles are mediated by environmental factors that turn genes on and off (McEwen, 2017), sometimes on a time scale of minutes. RDoC champions the notion that we need to study conventionally conceived psychological and biological phenomena together, not just as complements but as integrated phenomena, to understand how the psychological environment molds and alters the genetic endowment of each individual and indeed of each population. The following are responses to several misunderstandings we have encountered.

RDoC Does Not Foreground Biology at the Expense of Psychology

The declaration of the “Decade of the Brain” reflected a growing movement to emphasize biological phenomena and causes in many domains. NIMH championed this perspective, shifting funding away from behavioral research toward neuroscience, including physiological, pharmacological, and genetic phenomena. NIMH Directors asserted that “Mental illnesses are real, diagnosable, treatable brain disorders” (Hyman, 1998, p. 38) and that “mental disorders can be addressed as disorders of brain circuits” (Insel et al., 2010, p. 749).

That historical pendulum pushed NIMH rhetoric and policy to favor naïvely reductionistic approaches to psychopathology research for a considerable time, but RDoC has recentered the pendulum. Although there is concern that RDoC overweights biological phenomena (e.g., Goldfried, 2016; Lilienfeld, 2014; Lilienfeld & Treadway, 2016), in fact RDoC is carefully and explicitly agnostic about the mechanistic and causal relationships between psychology and biology and more radically advocates rigorous integration of the two domains (Berenbaum, 2014; Cuthbert & Kozak, 2014; Kozak & Cuthbert, 2016; Miller et al., 2016; Sanislow et al., 2010). Most obviously, examination of original or current versions of the RDoC Matrix (e.g., https://www.nimh.nih.gov/research-priorities/rdoc/constructs/rdoc-matrix.shtml) shows that some of its column headings and essentially all of its row

headings are psychological constructs. Cuthbert and Insel (2013, p.131) backed away from some earlier statements about the nature of mental illness as approached in RDoC that seemed untenably biologically reductionist and instead clarified that RDoC "is intended to provide a structure that places equal weight on behavioral functions and upon neural circuits and their constituent elements – that is, to be an integrative model rather than one based primarily on either behavior or neuroscience."

RDoC Does Not Eliminate Categorical Diagnosis in Favor of Dimensional Diagnosis

As the psychology research field has often faulted RDoC for a heavily biological bias, which in reality it does not have, the psychiatry research field has sometimes faulted RDoC for banishing categorical conceptualizations of psychopathology, which it does not do (Kozak & Cuthbert, 2016; Miller et al., 2016; Yee et al., 2015). "The RDoC initiative is intended to uncouple research questions from traditional diagnostic categories that are of limited validity and/or that are too heterogeneously large for productive validation against biological phenomena of smaller granularity." (Kozak & Cuthbert, 2016, p. 288). A potential outcome of RDoC is refinement of diagnostic categories but not their elimination. Cutpoints can be applied to dimensions, allowing dimensionally conceived measures or phenomena to be employed in categorical decision-making. An assumption of the RDoC initiative is that clinically significant phenomena are often continuous with milder, normative phenomena and that study of a range of severity can be informative. The value of this approach is especially apparent in the study of etiology. The time course of the development of features of disorder may vary considerably, and important psychological and biological changes may occur (and may be targets of pre-emptive intervention) before clinical presentation is conventionally diagnosable. The RDoC initiative leaves open when and how to employ dimensional or categorical constructs or approaches. Relative to the heritage of the DSM, this is indeed a shift toward dimensions but by no means an abandonment of categories.

RDoC Has Not Been Designed to Replace the DSM in Clinical Practice

Some critiques of the RDoC initiative fault it for being ill-prepared to achieve goals for which it was not designed, such as routine use in clinical practice (e.g., Weinberger et al., 2015), where third-party payers require binary decisions about need for treatment. RDoC certainly would not do well for that goal. How compatible the premises of the current insurance market are with optimal clinical practice will be better addressed when there is substantial progress in fleshing out and improving the RDoC approach. However, RDoC was not designed to replace the DSM in clinical practice (Lilienfeld & Treadway, 2016; Yee et al., 2015).

Granularity Matching Is Central to RDoC

In critiques of the DSM tradition (e.g., Beauchaine, & Klein, in press; Berenbaum, 2014; Hyman, 2010; Widiger & Clark, 2000; Yee et al., 2015), much has been made of the heterogeneity of DSM diagnostic categories, in terms of both etiology and symptoms, as an explanation for its limited progress across decades of research. NIMH leadership has

recently emphasized that RDoC was designed to right-size constructs and phenomena (Kozak, 2016; Kozak & Cuthbert, 2016). NIMH is predicting that better matching of the scope of psychological and biological phenomena and mechanisms, and better matching of those with diagnostic characterizations, will facilitate research progress. For example, some categories of symptoms, such as psychosis or mood, are transdiagnostic: thought disorder or depression can be prominent in a number of DSM diagnoses. But they may differ in quality or in the role they play as a function of other coincident symptoms, the time course or severity of those symptoms, or the developmental stage of the individual. Identifying the role of specific types of psychosis or mood, often measured on a continuum, will foster the development of RDoC. Conversely, the role of a given biological anomaly in psychopathology may depend on a host of factors. Rather than, for example, tallying how common a particular genetic finding is in a heterogeneous DSM disorder, RDoC favors finer-grained assessment of such relationships.

RDoC Foregrounds Psychophysiology

Psychophysiology, a discipline that crystalized in the early 1960s, subsumes nearly all of the research portfolio of what is now sometimes called human cognitive, affective, social, developmental, and clinical neuroscience. Most of psychophysiology involves one or more psychological independent variables, such as memory or anxiety, and one or more central or peripheral physiological dependent variables, such as functional magnetic resonance imaging or respiratory sinus arrhythmia (Fabiani, 2015; Miller, 2000; Stern, 1964). The RDoC matrix places psychophysiology at the center of its research strategy, with psychological constructs filling nearly all the rows and biological domains filling the majority of the columns (Infantolino, Crocker, Heller, Yee, & Miller, 2017; Miller et al., 2016). RDoC is intended to foster integration not only of psychological and biological measures but of psychological and biological constructs, potentially even resulting in hybrid constructs (Miller et al., 2016) as discussed below.

RDoC Is Compatible With Consideration of Developmental Phenomena

Weinberger et al. (2015, p. 1161) expressed concern that the RDoC matrix does not explicitly consider “the critical importance of time in defining course or prognosis and in clinical decision making.” But developmental aspects of the mechanisms, symptoms, and treatment of mental illness were considered from the inception of the RDoC initiative, including in the consensus conferences that played a central role in its creation (Kozak & Cuthbert, 2016). RDoC is neuroplasticity-friendly and presents no barriers to incorporation of constructs, and reliance on paradigms, that foreground developmental phenomena across any time scale (Morris & Cuthbert, 2012).

RDoC Is Compatible With Consideration of Cultural Factors

Similarly, nothing about RDoC obstructs consideration of environmental / contextual factors, including culture. The initial RDoC matrix does not include “culture” as a column of assessment, and perhaps it should (Berenbaum, 2013; Lilienfeld & Treadway, 2016). But concerns about cultural context are no more applicable to and no less important to consider

in relation to RDoC than to most of the conventional diagnostic tradition, which has focused on individuals, whether emphasizing intrapsychic processes, behavioral performance, or biological dysfunction.

RDoC Foregrounds the Endophenotype Construct

A decade or more ago, it was very common to hear "Now that we have the genome…", even before we had all of it. Now that the genome is in hand, it has become clear how inadequate "having the genome" is, by itself, in accounting for psychopathology (or mental phenomena more generally; Johnson, 2010). As noted above, the literature has been singularly unsuccessful in finding simple genetic explanations for psychopathology. Yet there is no question that genetic contributions to psychopathology are widespread. RDoC embraces the endophenotype construct, introduced to the psychopathology literature long ago by Gottesman and Shields (1972) as a potential bridge between genetic contributors and clinical manifestations of mental illness.

The inherently developmental endophenotype construct can be distinguished from a more generic construct, biomarkers, which Kozak and Cuthbert (2016) dismissed as lacking in meaning. They indicated that NIMH understands the term biomarkers to mean a directly biological measure and nothing more. Absent clear specification of the relationship of such a measure (or of any measure) to a hypothetical construct, finding a correlation between a biological measure and a clinical phenomenon is of little interest.

To date it has been difficult to meet the full set of endophenotype criteria that Gottesman and colleagues proposed, though there have been some successes (Iacono, Vaidyanathan, Vrieze, & Malone, 2014; Lenzenweger, 2010; Miller, Clayson, & Yee, 2014; Miller & Rockstroh, 2013; Patrick, Fowles, & Krueger, 2009). It may be time to reassess that framework and clarify what can be gained and by what means (Lilienfeld & Treadway, 2016). Iacono, Malone, and Vrieze (2017) proposed a compelling revision of the criteria, supporting the utility of the endophenotype concept and its fit within the RDoC approach (Lilienfeld, 2014; Miller et al., 2014). They advocate specific threshold criteria for what can qualify as an endophenotype, they suggest a strategy for endophenotype verification, and they discuss means of evaluating the utility of an endophenotype.

RDoC Fosters Hybrid Constructs

The biggest challenge that RDoC advocates is the development of essentially hybrid constructs. This goal goes well beyond mere clerical completion of the matrix, where (mostly) psychologically construed constructs intersect with (mostly) biological columns, though focus on a particular cell of the matrix by a particular project or researcher is not discouraged. Again, RDoC is intended to foster integration not only of psychological and biological measures but of the psychological and biological constructs those measures measure. As discussed in Miller et al. (2016), arousal is arguably the only construct in hand where that integration is successful – (a) where there are relatively well developed psychological and biological meanings of the term "arousal" and (b) where relationships between its psychological and biological mechanisms are also fairly well developed (even

though there is only limited consensus). Pursuit of this goal of hybrid constructs may involve the development of new tasks and measures, as well as new approaches to understanding causal mechanisms (e.g., Craver & Bechtel, 2007; Wright & Bechtel, in press).

RDoC serves as a projection target for many agendas. Even though it was developed very systematically, via a number of consensus conferences and other efforts, such an ambitious initiative was intended from the beginning to be evaluated and revised gradually as the literature – supportive and critical – develops. It is best implemented, critiqued, and improved when it is well understood.

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