COMMENTARY

The RDoC initiative and the structure of psychopathology

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Abstract
The NIMH Research Domain Criteria (RDoC) project represents a welcome effort to circumvent the limitations of psychiatric categories as phenotypes for psychopathology research. Here, we describe the hierarchical and dimensional structure of phenotypic psychopathology and illustrate how this structure provides phenotypes suitable for RDoC research on neural correlates of psychopathology. A hierarchical and dimensional approach to psychopathology phenotypes holds great promise for delineating connections between neuroscience constructs and the patterns of affect, cognition, and behavior that constitute manifest psychopathology.

The National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC) initiative represents a welcome effort to circumvent the well-documented limitations of psychiatric categories in psychopathology research. These limitations are addressed head-on in the two articles we were asked to contemplate in composing this commentary. Peter Lang, Lisa McTeague, and Margaret Bradley describe a multidecade program of research that was originally designed around psychiatric categories but, ultimately, delineates a fundamental psychobiological dimension underlying those categories. Kozak and Cuthbert outline how the limitations of psychiatric categories have led the NIMH to encourage movement away from research on psychiatric categories, and toward dimensional alternatives, under the auspices of the RDoC initiative.

In aiming to move psychopathology research away from categories defined by committee consensus and political processes, the NIMH has taken an important stand in favor of bringing science to bear on mental health. From a historical perspective, the current situation in psychopathology research affords some unique opportunities for progress. Traditionally, the NIMH sought to support research designed around psychiatric categories created by authority, particularly those defined in the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders (DSM). Now, changing its official perspective, the NIMH seeks to catalyze research focusing on basic biological mechanisms that undergird behavior. Improved articulation of those mechanisms should lead to a better understanding of how they go awry in psychopathology.

A fundamental challenge for the RDoC initiative relates to the phenotypic targets of biologically oriented research on psychopathology. What patterns of pathological behavior should we try to connect with basic biological mechanisms? If not psychiatric categories, then what phenotypes should frame our efforts? This is a critical question and requires rethinking some basic aspects of research design. In the previous era of authority-derived psychiatric categories, a traditional research design would entail studying biological variables in members of a psychiatric category and in comparison groups of participants matched on various covariates. The contribution from Lang et al. (2016) illustrates why this design is no longer tenable—we now know that psychopathology is not actually organized into DSM categories. Is there an alternative phenotypic organization that might facilitate biologically oriented psychopathological inquiry in the RDoC era?

Fortunately, an extensive body of research has emerged on an alternative phenotypic dimensional structure of psychopathology (Carragher, Krueger, Eaton, & Slade, 2015; Eaton, Rodriguez-Seijas, Carragher, & Krueger, 2015; Krueger & Eaton, 2015). The key task in the RDoC era is to integrate this dimensional structure with indicators of variation in the parameters of underlying biological mechanisms. Indeed, this perspective is now specified explicitly on NIMH’s RDoC webpage (http://www.nimh.nih.gov/research-priorities/rdoc/rdoc-frequently-asked-questions-faq.shtml):

Mental disorders involve both psychological and biological components. That is why subjective experience and the questionnaires that measure them are a significant part of the RDoC matrix. In fact, the five major domains are based on prior work that has tried to understand human behavior using a variety of methods such as temperament and personality measures, and structural analyses of the patterning among multiple mental disorders (e.g., internalizing vs. externalizing, Big Five or Big Three, etc.). RDoC is an attempt to explore the biological systems relating to these psychological constructs starting with the knowledge we already have.

Hence, the remainder of this commentary focuses on a very brief review of key findings from the literature on the dimensional...
The broad outlines of the hierarchical-dimensional structure of psychopathology have been delineated. One major concern in shifting from the categorical DSM framework for psychopathology to a dimensional framework involves knowing what the alternative dimensional framework might look like. Fortunately, a substantial literature points to essential elements of the framework portrayed in Figure 1. In this figure, the numbered constructs represent dimensions of individual differences in specific psychopathological tendencies, and these tendencies are arranged in a hierarchy based on their patterns of covariation. For example, a broad externalizing tendency subdivides into more antagonistic and more disinhibited patterns of behavior.

The hierarchal nature of this model clarifies a key aspect of the paragraph from the RDoC website quoted earlier. Rather than being forced to choose among models with differing numbers of major dimensions, researchers should realize that these models are related to each other in a systematic hierarchy and, thus, are all part of the single larger model depicted in Figure 1. The concept of hierarchy helps in articulating how constructs can be simultaneously heterogeneous and homogeneous and how biological mechanisms of different breadth are likely to be influential at differing levels of the hierarchy. Some biological mechanisms are likely to influence brain function very broadly and, thus, to cause variation homogeneously in upper-level dimensions, whereas other mechanisms are likely to influence more specific brain functions and, thus, to cause variation in lower-level subdimensions. For example, serotonin is implicated broadly in externalizing tendencies, and, thus, Antagonism and Disinhibition may covary in part because both are influenced by global levels of serotonin (Allen & DeYoung, in press; DeYoung, Peterson, Séguin, & Tremblay, 2008). Other brain mechanisms differentiate Antagonism and Disinhibition, however, as we illustrate in an example in our third point below.

2. The hierarchical-dimensional structure of psychopathology can be seen in data from multiple instruments and multiple reporters.

Figure 1 is reprinted from a paper focusing on the DSM-5’s new dimensional model of maladaptive personality variation and on an instrument designed to operationalize that model, the Personality Inventory for DSM-5 (PID-5; Krueger, Derringer, Markon, Watson, & Skodol, 2012). However, it is essential to point out that the organization in Figure 1 does not reflect one single and specific measurement instrument. Rather, the constructs in the figure can be assessed by different instruments, and the properties of those instruments determine how well they can assess differing aspects of the construct hierarchy in the figure. For example, DSM categories that have relatively greater variance in the population at large (i.e., those with a relatively higher prevalence, such as mood, anxiety, substance use, and antisocial disorders) delineate dimensions at the top two levels of the Figure 1 hierarchy, whereas the overall propensity to psychopathology can be subdivided into internalizing and externalizing dimensions (Krueger & Eaton, 2015). More detailed distinctions at lower levels of the hierarchy are not optimally assessed by the DSM’s diagnostic dichotomies because detailed information about specific signs and symptoms is collapsed into variables that can take on only one of two values (i.e., 0 = diagnosis absent vs. 1 = diagnosis present) (Krueger & Finger, 2001). In contrast, by analyzing specific symptoms that are not preaggregated into the diagnostic dichotomies that the NIMH has rightly rejected as scientifically inadequate, a more detailed hierarchy is revealed. Working with specific symptoms enables delineating finer-grained elements that, nevertheless, coalesce into the dimensions seen in Figure 1 (e.g., Markon, 2010; Wright & Simms, 2015).

In addition, the Figure 1 model is not limited to self-report data. To pick a specific example, the DSM-5 maladaptive traits can also be assessed by lay informants or by clinicians, and data from both types of reporters generally reveal the structure portrayed in Figure 1 (Markon, Quilty, Bagby, & Krueger, 2013; Morey, Krueger, & Skodol, 2013). This generality of structure across reporters is a well-replicated finding that is seen in data on more maladaptive (Rescorla et al., 2012) and more adaptive (DeYoung, 2006) individual differences. Importantly, therefore, the assessment measures that have been found to yield the Figure 1 model include indicators of objective behavior (e.g., observation-based descriptive accounts), not merely subjective experience. Thus, one can reasonably consider Figure 1 to reflect the structure of psychopathological behavior and use it to guide research into the biological mechanisms underlying that behavior.

3. A hierarchical-dimensional approach to psychopathology phenotypes is helpful in delineating neural correlates of psychopathology.

RDoC seeks to propel psychopathology research forward by shifting to a dimensional approach to characterizing individual differences and, also, by focusing on biologically informative research on mechanisms underlying those individual differences. In embracing this approach, we would like to highlight the multivariate aspects of the RDoC initiative. The organization of the RDoC matrix into broad domains naturally leads to questions of generality and specificity of psychobiological mechanisms. A multivariate psychobiological approach is likely to be considerably more informative than research designs that compare
category members with control participants because issues of specificity versus generality are naturally highlighted and rendered tractable.

We highlight here a recent multivariate psychobiological project on which the authors of this commentary collaborated, simply as one illustration of this type of approach and its potential advantages. This work also serves as a complement to the contribution from Lang and colleagues, in the sense that we focused on externalizing phenomena, whereas Lang and colleagues focused on internalizing phenomena.

Abram, Wisner, Grazioplene, Krueger, MacDonald, and DeYoung (in press) worked with resting state fMRI data from a community sample ($N = 244$) to test hypotheses about the relevance of the insula to externalizing behaviors. Independent components analysis was applied to resting state fMRI data, and three intrinsic connectivity networks (ICNs) were derived that overlapped significantly with the insula. In addition, participants were phenotyped by using an abbreviated form of the Externalizing Spectrum Inventory (ESI) (Krueger, Markon, Patrick, Benning, & Kramer, 2007; Patrick, Kramer, Krueger, & Markon, 2013a). The ESI assesses externalizing tendencies, which, as portrayed in Figure 1, tend to subdivide into more disinhibited and more antagonistic (callous aggression) components, as well as encompassing specific tendencies toward substance misuse. Unlike a classical cases versus controls design, this large-N dimensional assessment design provided opportunities to implement a multivariate psychobiological approach, allowing us to test whether specific insula networks were (and were not) associated with specific externalizing phenotypes, with reasonable power to discern both convergent and discriminant relationships, given the sample size.

We found that posterior insula network coherence positively predicted both disinhibition and substance abuse. By contrast, coherence in a network encompassing the anterior insula, ventral striatum, and anterior cingulate was negatively associated with disinhibition. In addition, coherence of insula networks did not relate to the callous aggression dimension as indexed by the ESI. Moreover, we presented evidence for the specificity of insula ICNs in relation to disinhibition and substance abuse as compared to other frontal and limbic ICNs. That is, frontal and limbic ICNs containing fewer insula voxels were not significantly predictive of externalizing tendencies.

From a design perspective, we wish to emphasize how this multivariate-psychobiological research approach provided evidence for both neural specificity and phenotypic specificity. By studying externalizing phenomena in terms of a dimensional phenotypic model (as opposed to cases vs. controls), along with focusing on individual differences in differentiable neural networks, we were able to adduce evidence for the specific role of insula networks in specific externalizing tendencies (i.e., those associated with impulsive-irresponsible tendencies as opposed to callous aggressive behavior).

Nevertheless, there were a number of key limitations of this work. Phenotypic assessment was limited to self-report, and we focused on one type of fMRI data (resting-state coherence, which could be usefully augmented with other MRI data, such as structural data, task-derived functional data, diffusion tensor imaging, etc.). Efforts to model different biological variables simultaneously, as indicators of coherent constructs, are likely to yield even stronger and clearer models of the connections among biological and psychometric indicators of individual differences. Patrick and colleagues (2013b) have described this as a psychoneurometric approach and have illustrated the utility of this approach in studying externalizing phenomena.

In sum, as the contribution from Lang and colleagues clearly illustrates, many research groups are now converging on multivariate psychobiological approaches, facilitated by the RDoC framework. We look forward, in particular, to learning more about the newly funded RDoC project they describe in their paper. Indeed, bringing research groups together is likely to be the key to establishing real traction in RDoC-oriented research, as illustrated, for example, by contemporary collaborative research on the molecular genetics of human individual differences (see, e.g., Rietveld et al., 2013). Along these lines, the recently launched RDoC database (http://rdocdb.nimh.nih.gov/) is likely to prove helpful in combining and synthesizing findings across differing lines of ongoing RDoC research. As Kozak and Cuthbert (2016) discuss, these are changing times, and also exciting times, in the biological study of psychopathology—thanks in no small part to the RDoC initiative.

References


Markon, K. E. (2010). Modeling psychopathology structure: A symptom-comorbidity approach and have illustrated the utility of this approach in studying externalizing phenomena.

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