

NATIONAL INSTITUTE OF MENTAL HEALTH



NIMH Research Domain Criteria (RDoC) Initiative: Development and Environment in RDoC Workshop Proceedings and Thematic Summary

November 18–19, 2019



National Institute
of Mental Health

U.S. Department of Health and Human Services
Public Health Service
National Institutes of Health
National Institute of Mental Health



TABLE OF CONTENTS

Introduction.....	2
Background	2
Purpose	2
Integrating Development and Environment in RDoC	3
Breakout group discussions	3
Large group discussion.....	4
Using RDoC as a Tool for Research and Review	6
Considerations for investigators, reviewers, and the grant application process	6
Investigators	6
The grant application process	6
Study design considerations	7
Development studies	7
Environment studies	7
Depicting and Messaging RDoC.....	8
Developing a visual	8
Potential strategies to enhance communication about RDoC	8

Introduction

Background

Research Domain Criteria (RDoC) is an ongoing initiative to explore psychopathology based on dimensions of observable behavior and neurobiological measures. Developed to fulfill one of the National Institute of Mental Health's (NIMH) objectives in its 2008 Strategic Plan, to "define the mechanisms of complex behavior," RDoC provides a framework to investigate fundamental biobehavioral mechanisms and components that may span multiple disorders and to identify the full range of normal variation in human behavior and cognition. The concept is designed to integrate genetic, neurobiological, behavioral, environmental, and experiential measures, ultimately enabling the development of reliable, valid measures for use in basic and clinical studies.

The intent of RDoC is not to supersede existing diagnostic tools; indeed, RDoC itself is not a diagnostic manual. Rather, it is a set of principles and framework that provides investigators with an alternative transdiagnostic, translational system for understanding psychopathology. In recent years, clinicians and investigators have identified a number of challenges to using current diagnostic tools, such as the *DSM-5* or *ICD-10*. Such diagnostic classifications, now generally understood to represent heterogeneous syndromes, have proven to be problematic in incorporating prognostic or predictive biomarkers or to accommodate significant advances in diagnostic science. Moreover, the manner in which such classification manuals are used tends to reify the disorders listed in them as specific, discrete entities.

RDoC addresses these gaps by focusing more narrowly on dimensional functions and neural circuits as they relate to the dysfunction and dysregulation associated with mental disorders. To do so, RDoC requires that its concepts meet a set of equally weighted twin criteria: evidence for a functional dimension of behavior or cognition, and evidence for a specific neural system involved in this functional dimension. These concepts are organized within a two-dimensional matrix framework. The current iteration of this matrix specifies six primary *domains* of human cognition and behavior (including Negative Valence Systems, Positive Valence Systems, Cognitive Systems, Systems for Social Processes, Sensorimotor Systems, and Arousal/Regulatory Systems). Each functional domain contains a set of *constructs*, which represent individual mechanisms, processes, and other aspects. The matrix also delineates *units of analysis*, i.e., a diverse array of tools and methods to measure each construct (currently including Genes, Molecules, Cells, Circuits, Physiology, Behavioral Assessments, Self-Report, and Paradigms). All aspects of the matrix are considered as examples of the principles and framework, as elements are intended to evolve as research findings accrue.

Purpose

Developmental trajectories across the life span are a significant element of the RDoC system—not only for the pursuit of a more comprehensive understanding of psychopathology, but also for the instantiation of early prevention and intervention



strategies. Similarly, environmental factors also are included within the RDoC framework and are widely understood to influence the development of mental illness, with significant, bidirectional risk and protective factors between the two.

Despite these fundamental roles in the overall RDoC framework, Development and Environment currently are absent from the RDoC matrix, which is only one aspect of RDoC; instead, notes about these essential elements are briefly addressed on a [separate webpage](#). The RDoC Unit at NIMH therefore identified a need to delineate and integrate Development and Environment more holistically within the framework to provide sufficient guidance for investigators whose research interests are centered on these topics. To this end, NIMH convened a workshop of leading experts to propose and discuss potential ways to update the RDoC framework to include more extensive coverage of Development and Environment. Unlike some previous RDoC workgroups, which were intended to designate and formalize new components for implementation in the RDoC matrix, the Development and Environment Workshop was not a formal Advisory Council workgroup; instead, the workshop deliberations will serve to inform future efforts. As part of the introduction, Dr. Bruce Cuthbert, Director of the RDoC Unit, encouraged workshop members to brainstorm creative, big-picture solutions rather than fine-grain practical details.

Workshop members also were tasked with discussing RDoC's role as a tool for research and review. While primarily intended as a system for understanding and exploring the spectrum of human functioning, RDoC is also designed to serve as an alternative standard for peer review. This purpose is in response to the fact that current diagnostic categories (i.e., *DSM*- or *ICD*-specified entities) historically have driven the entire clinical research system for mental disorders, including study sections, journals, trials, and regulatory agencies. The RDoC initiative enables investigators to approach clinical research from a perspective based on behavioral neuroscience, unconstrained by such classification systems.

With these goals in mind, workshop members formed small breakout groups to discuss three topics: (1) explicating Development and Environment in RDoC, (2) developing experimental designs using RDoC, and (3) depicting and messaging RDoC. After each breakout session, the attendees reconvened to share and consider their ideas. The following material thematically summarizes the content of these discussions.

Integrating Development and Environment in RDoC

Breakout group discussions

The workshop attendees split into small groups to discuss in turn specific topics related to integrating Development and Environment into the RDoC framework. They reconvened to report their discussion points to the full workshop, summarized below:



Group topic	Discussion points
Development/Environment and externalizing	<ul style="list-style-type: none"> • Specify active ingredients of the environment, conceptualizing environment with similar complexity as existing RDoC constructs. • Remember that environment is broad and dynamic—it is critical to balance these considerations with an appropriate level of detail and dimensionality. • Use developmental timing to understand adaptation, and recognize that the complexity of these interactions may not be captured in a single grid or matrix. • Account for constancy and change across development. • Equally weight phenotypic and quantitative measures. • Use matrices judiciously.
Development/Environment and internalizing	<ul style="list-style-type: none"> • Articulate environmental and developmental domains more explicitly, treating them as core process mechanisms, mediators, and monitors. • Recognize development as a mechanistic, multi-trajectory process with specific outcomes. • Develop advanced methodologies and modeling strategies, and ensure reviewers are equipped to understand them. • Use variability and scatter to understand normative development and personalized approaches to psychopathology. • Capture interactions across development and environment, including further specification of social-interpersonal domains and attachments.
Development/Environment and cognitive/affective processes	<ul style="list-style-type: none"> • Ensure that rich detail does not constrain investigators. • Use RDoC to facilitate a common language among investigators and reviewers. • Consider aspects of development/environment that are already represented in existing RDoC domains (e.g., high degree of overlap between social processes domain and environment). • Consider challenges in undertaking longitudinal development-focused studies within the current R01 grant structure.
Development/Environment and social processes	<ul style="list-style-type: none"> • Detail a set of RDoC-adjacent or -affiliated “expansion packs” for development and environment. • Consider social processes contextually, with attention to paradigms and to embeddedness in layered milieus. • Understand development and environment as both outcomes and influences. • Encourage emphasis and momentum for a developmental perspective throughout the life span—not just pediatric populations. • Rely on existing conceptual frameworks where possible. • Recognize that salient transition points vary dramatically by sociocultural context.

Large group discussion

Together, the workshop attendees addressed the considerations presented by each breakout discussion group. Consensus among all discussants was that a successful RDoC framework must integrate Development and Environment with an appropriate degree of richness and detail, striking a balance between under-specification and constraint. However, workshop participants disagreed on an optimal approach to achieve this balance. Their proposed strategies for including Development and Environment in

the RDoC matrix generally fell along a spectrum from lowest to highest degree of integration and specification.

At the lowest end of integration, some participants advocated for a vector model, which might display an arrow for each RDoC construct to visually represent how concepts of Development and Environment interact. The goal is to stimulate thought by visually representing these concepts, encouraging investigators to develop and define dimensions of Development and Environment they consider to be relevant. Other participants critiqued this model for not sufficiently modifying the matrix or satisfying investigators who specialize in these topics.

At the high end of integration and specification, some participants recommended developing distinct matrices for Development and Environment, to be nested within the existing RDoC matrix or to be considered separately. Other workshop attendees cautioned against overcomplicating the system and advised maintaining a single RDoC matrix for universal use by all investigators. (Investigators who are not interested in Development or Environment can simply ignore irrelevant aspects of the matrix.) However, some participants who argued for one matrix felt that the certain aspects of the current matrix might be incompatible with capturing all aspects of Development. They opined that many of the constructs and domains were developed with consideration of adult functioning. Therefore, they argued that ex post facto additions to the matrix might not adequately capture developmental trajectories from infancy to adulthood, and felt that some domains might have to be reconceived from a developmental perspective.

Most participants' ideas occupied a space between these extremes. They felt that concepts of Development and Environment should be specified with the same detail as other existing constructs, and suggested that NIMH begin by articulating a dimensional approach to Development and Environment that could inform the creation of new relevant domains or columns within the RDoC matrix. The participants agreed that the RDoC Unit can best convey the importance of Development and Environment by incorporating these concepts with a high degree of detail and prominence (e.g., by adding a note under relevant constructs that brain region development is sensitive to maternal nicotine exposure and by linking to a pre-built PubMed search result with available information about these processes), rather than by affixing superficial visual representations. The workshop participants agreed that, when possible, RDoC should avoid overcomplication by relying on well-validated conceptual paradigms and frameworks.

Although their proposed solutions for integrating Development and Environment were diverse and, at times, oppositional, workshop attendees generally agreed that the two concepts are significantly interrelated and should not be artificially separated within the matrix.

Using RDoC as a Tool for Research and Review

The workshop participants broke into small groups to formulate exemplar study designs using potential RDoC Development and Environment constructs. Then, they reconvened to discuss the theoretical challenges, benefits, and solutions they encountered in their small groups.

Considerations for investigators, reviewers, and the grant application process

Investigators

Consensus among discussants was that many development- and environment-focused investigators feel excluded or ignored by the RDoC system. Although the RDoC webpage explicates NIMH's perspective that Development and Environment are critical elements of the RDoC framework, the absence of these concepts from the RDoC matrix itself has led some investigators to feel that their research areas are underrepresented or undervalued. Workshop participants agreed that NIMH can best convey the importance of Development and Environment by specifying these elements to the same degree as existing constructs.

Workshop attendees further agreed that RDoC must balance guidance with constraint. That is, RDoC must specify Development and Environment with enough detail to support and inspire investigators in their research, without miscommunicating that investigators must incorporate every concept. For example, an investigator studying a given environmental influence should understand that their research need not address threat, trauma, parenting, *and* school context simply because RDoC specifies these constructs under Environment. Discussants disagreed on a best approach to resolve this concern. Some proposed that the RDoC initiative should maximize the detail and richness of developmental and environmental dimensions to clarify that investigators should not aim to address every construct or subconstruct. Other discussants disagreed, pointing out that overcomplicating and over-specifying the framework may convey an inappropriate degree of precision, which could be interpreted as constraining and could lead to confusion.

The grant application process

Broad consensus among discussants was that there are challenges in undertaking longitudinal studies within the current R01 grant structure. They noted that an RDoC-based developmental study would enable investigators to capture the richness of developmental processes and their potential mechanistic influences, but this might require a significantly longer funding period than R01 grants provide. Some workshop participants suggested using secondary data analysis or mining from existing data sets—such as the [Adolescent Brain Cognitive Development \(ABCD\) Study](#)—but conceded that these large-scale studies currently lack adequate depth and detail to allow analysis of finer-grained, transdiagnostic concepts captured by RDoC. No conclusive solution was reached on these issues.



Study design considerations

Development studies

The workshop participants recognized the value of the RDoC system for enabling investigators to analyze children's risk factors before they are old enough for formal diagnosis. The RDoC framework is well suited for a developmental understanding of psychopathology, which often targets mechanistic risk factors rather than categorical diagnoses. This approach aligns with NIMH's mission to identify people early in the developmental course who are at risk for psychopathology, enabling investigators to develop early prevention and intervention efforts.

Some participants reported difficulties conforming their developmental study designs to fit RDoC-specific constructs, despite feeling that their studies should be highly compatible with the RDoC framework. They noted that RDoC training modules may increase investigators' comfort with the system. They added that although RDoC is well suited to developmental approaches to psychopathology, the matrix in its current form was perceived as having several constructs that are adult-based.

One challenge communicated by attendees was difficulty designing developmental studies without a target phenotype upon which to map outcomes. One participant suggested that a new column within the RDoC matrix for "Impairment/Functioning," which would dimensionally target timepoints with sustained impairment to functioning, may help investigators advance clinically meaningful phenotypes without relying on *DSM*-based categories. Other participants disagreed that end phenotypes are at issue, pointing out that RDoC encourages a bottom-up approach (based on neurodevelopmental and behavioral trajectories) rather than a top-down approach (working backward from a prespecified outcome).

Environment studies

Participants who designed environmental RDoC studies found that the matrix can flexibly accommodate key Environment dimensions (such as threat, safety, cognitive stimulation, physical exposure, and predictability), and that these dimensions can interrelate neatly under existing RDoC domains, such as Negative Valence. However, the natural overlap of potential dimensions under Environment with existing constructs within existing domains may overcomplicate the matrix, necessitating careful thought about how to represent interrelationships among these aspects.

They pointed out that the high degree of compatibility between RDoC and Environment presents a valuable opportunity to examine how environmental factors (such as peer deviance or parental monitoring, perhaps organized as dimensions under the Social Processes domain) further contribute to or moderate associations between developmental trajectories and subsequent psychopathology. Participants also proposed controlled study designs informed by RDoC principles in which hypothesized environmental mechanisms are manipulated and the behavioral effects and associated brain changes are measured. The results of such a study, in turn, may inform the organizing principles and structure of the RDoC framework.

Workshop attendees expressed concern that some aspects of Environment may fall outside the purview of NIMH; for example, grant applications focused primarily on school outcomes are assigned to NICHD, even if they involve mental health. Program staff present at the workshop clarified that the assignment of applications (including those that use an RDoC approach) to NIH institutes is carried out according to [application referral guidelines of NIH](#). (Also see <https://public.csr.nih.gov/ForApplicants/SubmissionAndAssignment/DRR/assignmentprocess>.)

Depicting and Messaging RDoC

Developing a visual

Meeting participants broke into small groups to discuss visual representations of the RDoC framework, including aspects of Development and Environment. Although not intended for actual use, the RDoC Unit hoped that expert opinions about pictorial depictions of RDoC will guide further messaging and development of the RDoC matrix.

In general, the discussants (particularly those whose work involves development) agreed that when differentiating childhood from adulthood, RDoC must clarify that constructs are not “blurry” or “unformed” in childhood—they are merely different from adulthood. Others also pointed out that there may be minimal differentiation between constructs in prenatal development, but that divergent trajectories may occur over the course of development, and that constructs in one domain could influence those in another. However, because exact developmental timepoints along some of these trajectories are currently unknown, RDoC should avoid visually representing them.

Participants also debated how best to depict the influence of environment. Suggestions included representing environment in its own matrix, including environment as a vector arrow along the bottom, or showing environment as a conceptual mechanism influencing processes within the larger RDoC matrix.

Finally, the attendees encouraged the RDoC Unit to consider animating the visual representation in video or .gif form.

Potential strategies to enhance communication about RDoC

Workshop participants agreed that some resistance to RDoC is the result of insufficient messaging among investigators, reviewers, and other stakeholders. They had a number of suggestions for increasing and enhancing communications about RDoC, including:

- Continue attendance at conferences focused on developmental and environmental considerations of mental health.
- Continue to offer webinars, presentations, and to publish articles on the RDoC initiative.
- Provide training for new investigators on the principles of RDoC.



- Highlight well-validated constructs that may be similar across development for investigators.

In 2020 and beyond, NIMH will continue its work to improve, expand, and share the RDoC system along these lines. The RDoC Unit intends to use the valuable expert opinions and advice gathered from the participants in this “Development and Environment in RDoC” Workshop to inform the development of future iterations of the framework and RDoC-affiliated initiatives.