

Special Issue Editorial

Using development and psychopathology principles to inform the Research Domain Criteria (RDoC) framework

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Abstract

In 2010, the Research Domain Criteria (RDoC) were developed to advance our understanding of the pathophysiology of mental illness across multiple levels of analysis, ranging from cells to circuits to self-report instruments. Several conceptual RDoC-informed manuscripts have highlighted the importance of studying how developmental processes give rise to psychopathology. However, there are few empirical studies that integrate the RDoC framework with development and psychopathology principles. This special issue was developed to fill this empirical gap. In this introduction to the special issue, we describe how the developmental psychopathology field predates and informs the RDoC framework. We highlight three important ways in which developmental psychopathology and the RDoC framework can mutually inform one another, leading to novel discoveries to identify, prevent, and treat mental health problems across the life span.

Keywords: research domain criteria, development and psychopathology, development

(Received 6 July 2021; revised 7 July 2021; accepted 8 July 2021)

In 1984, Cicchetti described diverging interests between psychiatrists, who diagnosed and treated individual patients, and academic researchers, who conducted controlled experiments in their laboratories with little thought to the real-world implications of their work (Cicchetti, 1984). While researchers thought carefully about developmental processes and attempted to study these in the laboratory, clinicians at the time rarely considered how the study of typical developmental processes could be used to understand emerging symptoms of psychopathology (Cicchetti, 1984). Clinicians and the researchers each made important contributions toward advancing the science and treatment of psychiatric disorders, but they had no common, developmentally informed scientific language they could use to share their discoveries. The field of development and psychopathology was created, in part, to bridge this gap between clinicians and academic psychologists by providing a theoretical framework to support the bidirectional communication between researchers and clinicians (Cicchetti, 1984).

In many ways, the 2010 advent of the Research Domain Criteria (RDoC) recapitulates this tension between clinical research and practice (Insel, 2009; Insel et al., 2010). RDoC was developed to provide a language for researchers to advance understanding of the pathophysiology of mental illness, one that is not constrained by diagnostic boundaries (Insel et al., 2010). It is

expected that RDoC-informed research will result in novel methods of classifying mental illness based on a dimensional approach and that it could result in the development of an empirically informed system for classifying mental illness (Insel et al., 2010). Mirroring the lack of attention paid to developmental processes in the psychiatric literature in the 1980s, within the RDoC framework there is currently little consideration of basic developmental processes or the broader context in which children develop (Beauchaine & Hinshaw, 2020; Boyce et al., 1998; Cicchetti & Aber, 1998; Franklin, Jamieson, Glenn, & Nock, 2015; Garber & Bradshaw, 2020). Although it is a central aim of RDoC to promote our understanding of neurodevelopmental origins of mental illness (Morris & Cuthbert, 2012), few empirical studies have attempted to integrate developmental principles into the existing RDoC framework (Beauchaine & Hinshaw, 2020; Franklin et al., 2015; Garber & Bradshaw, 2020; Mittal & Wakschlag, 2017; Smith & Pollak, 2020).

This lack of attention to developmental principles in RDoC does not mean that the RDoC perspective in children has been ignored. The origins of developmental and dimensional perspectives on psychopathology began in the 1960s when Achenbach began studying symptoms of child psychopathology (Achenbach, 1966; Cicchetti, 1984; Sroufe, 2009), and laid the foundation for the field of development and psychopathology (Cicchetti, 1984). During this time Achenbach and colleagues were describing the importance of using dimensional methods of categorizing child behavior (Achenbach, 1966), Cicchetti advocated for the inclusion of a multiple levels of analysis perspective in studies of child behavior (Cicchetti, 1984; Cicchetti & Dawson, 2002; Sroufe & Rutter, 1984), and the importance of identifying

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Cite this article: Conradt E, Crowell SE, Cicchetti D (2021). Using development and psychopathology principles to inform the Research Domain Criteria (RDoC) framework. *Development and Psychopathology* 33, 1521–1525. <https://doi.org/10.1017/S0954579421000985>

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causal mechanisms was emphasized by Sroufe and Rutter (Rutter & Sroufe, 2000; Sroufe & Rutter, 1984). The development and psychopathology field predates RDoC and is therefore a field that is uniquely positioned to integrate life span development with the RDoC framework.

A key goal of the field of development and psychopathology was to, “yield a classification system informed by empirical study of individual development from the ground up, rather than simply a downward extension of adult categories of disturbance or acceptance of clinic-derived child entities.” (Sroufe, 2009). In other words, a simple transition from “RDoC for adults” to “RDoC for children” could hinder and confuse our understanding of pathophysiological mechanisms of psychopathology. In this editorial, we highlight three important ways in which a developmental psychopathology perspective can further inform RDoC and advance our understanding of the developmental origins of mental illness.

Improved Measurement of Adaptive Developmental Trajectories Will Inform Risk Trajectories

A hallmark of the development and psychopathology perspective is rigorous measurement of typical developmental trajectories, which can be used to inform how development goes awry (Sroufe & Rutter, 1984). As articulated in the 1980s, “we can learn more about the normal functioning of an organism by studying its pathology and, likewise, more about its pathology by studying its normal condition.” (Cicchetti, 1984, p. 1). Children are not born with complex forms of psychopathology. Instead, symptoms of psychopathology “are complex products of development” (Sroufe, 2009). Developmental psychopathologists have been studying adaptive developmental trajectories of behavior, beginning in infancy, since the landmark Minnesota Longitudinal Study of Parents and Children in 1975 (Sroufe, Egeland, Carlson, & Collins, 2009). Data from the Minnesota Longitudinal Study allowed psychologists to study risk and resilience (Pianta, Egeland, & Hyatt, 1986), continuities and discontinuities in development (Englund, Kuo, Puig, & Collins, 2011), and the dynamic ways in which parents and children interact to increase risk for psychopathology across the life span and across generations (Carlson, Jacobvitz, & Sroufe, 1995; Farber, Vaughn, & Egeland, 1981; Lorber & Egeland, 2009; Roisman, Aguilar, & Egeland, 2004). This study laid the foundation for developmental psychopathology principles to be empirically tested for the first time.

It is typically assumed that youth “grow into” psychopathology. Instead, developmental processes provide an opportunity to “grow out” of psychopathology risk, through improvements in self-regulation and other foundational skills (Cicchetti & Tucker, 1994). For example, it is expected that toddlers will tantrum and fuss when they are prevented from playing with a desired (but perhaps dangerous) object. However, an adult who is enraged when his/her goals are blocked shows a more concerning pattern of behavior that could be indicative of significant psychopathology, such as a personality disorder. A development and psychopathology perspective shows that this kind of homotypic continuity exists and may help us identify vulnerable children before the emergence of complex forms of psychopathology (Franklin *et al.*, 2015; Mittal & Wakschlag, 2017; Rutter & Sroufe, 2000).

To prevent maladaptive trajectories, we need studies that begin in early childhood and that model typical and atypical trajectories of RDoC-informed traits. Exemplary work of this kind comes

from research modeling the development of irritability in early childhood (Wakschlag *et al.*, 2015, 2020). In this research, irritability – a construct that can be measured at birth and throughout the life span – is measured using a multiple levels of analysis perspective (neurobiology, psychophysiology, behavioral observation, parent report) to identify the specific constellation of symptoms that may predict psychopathology (Wakschlag *et al.*, 2015, 2020). As described by Luby, Wakschlag, and colleagues, the ultimate goal of these studies is to develop data-driven algorithms that may help pediatricians and parents identify young children who may be vulnerable to neurodevelopmental delay and/or problem behavior (Luby *et al.*, 2019). As described in this special issue, RDoC and developmentally informed data may be leveraged to generate mental health risk calculators for use in pediatric and mental health clinics to better identify and prevent emerging psychopathology in the first years of life (MacNeill *et al.*, this issue).

Given that psychopathology is not present at birth, developmental psychopathologists have had to take a dimensional approach to modeling developmental risk trajectories (Achenbach, 1966; Mittal & Wakschlag, 2017). Already in 1981 this study design was deemed a necessity when Cicchetti and Rizley wrote about the study of child maltreatment: “any classification or nosology represents a rather futile effort to divide what is in reality a continuum into discrete categories...failure to attend to this major source of heterogeneity runs the very real risk of ignoring a source of variation that is crucial to an appreciation of the differing etiologies, sequelae, intergenerational transmission patterns, and treatment responses of different types of maltreatment.” (Cicchetti & Rizley, 1981, p. 2). To study the etiology of psychiatric disorders using an RDoC framework it may be beneficial to focus on the development of traits known to be expressed in both childhood and adulthood, such as impulsivity (Beauchaine & Hinshaw, 2020), irritability (Wakschlag *et al.*, 2015), or emotion dysregulation (Beauchaine & Cicchetti, 2019; Ostlund *et al.*, 2019) to improve early identification of risk for psychopathology.

By studying developmental trajectories dimensionally we are better equipped to model the nonlinear and dynamic nature of these trajectories, which could help identify risk trajectories (Sroufe, 2009). For example, neurobehavioral disinhibition is a transdiagnostic construct (found across a wide range of disorders; Garvey, Avenevoli, & Anderson, 2016) that is elevated in adolescents with complex psychopathology, ranging from conduct disorder to cognitive impairment and problems with self-regulation (Iacono, Malone, & McGue, 2008). Fisher and colleagues found that prenatal substance exposure predicted increases in neurobehavioral disinhibition from age 8 to 14 and early life stress predicted executive functioning difficulties, a component of neurobehavioral disinhibition (Fisher *et al.*, 2011). These findings show that we may be able to identify specific risk trajectories (in this example trajectories that include early life stress and prenatal substance exposure) when transdiagnostic traits are measured across sensitive periods of development.

By modeling adaptive and maladaptive developmental trajectories, developmental psychopathologists have found that different symptom clusters could have different developmental time courses (Casey, Oliveri, & Insel, 2014; Franklin *et al.*, 2015). For example in this special issue Karalunas and colleagues use innovative longitudinal network models to show that for some children with working memory impairments, symptoms of attention-deficit/hyperactivity disorder (ADHD) in childhood lead to risk for the development of depression in adolescence (Karalunas *et al.*, this issue). It was only by modeling

RDoC-informed constructs (working memory impairment) across childhood that these authors were able to identify specific factors that contributed to depression risk in adolescence. Therefore identifying continuities and discontinuities across development shows us that a complete understanding of the etiology of disorder using an RDoC approach should measure how these risk processes change over time (Franklin et al., 2015; Lebowitz, Gee, Pine, & Silverman, 2018), and consider equi- and multifinal processes.

Measurement of Equi- and Multifinality using RDoC-Relevant Constructs may Lead to Improvements in Early Identification and Prevention of Psychopathology

An explicit focus on dimensional constructs that originate early in development will allow us to better model processes of equi- and multifinality. Psychopathology is etiologically complex and many diverse developmental pathways can result in the same disorder, a concept known as equifinality (Cicchetti & Rogosch, 1996). By definition, developmental studies that include repeated multilevel assessments of risk factors thought to predict psychopathology are needed to examine equifinal processes. For example, in this special issue Ostlund and colleagues examine how prenatal substance exposure, maternal hostility, and observed/parent report of temperament in infancy can be examined to predict externalizing and internalizing behavior in early childhood (Ostlund et al., this issue). They find specific equifinal pathways to risk for internalizing and externalizing behavior in preschoolers that include both prenatal substance exposure and maternal hostility (Ostlund et al., this issue).

With multifinal processes, a variety of different disorders may emerge as a result of similar early life histories (Cicchetti & Rogosch, 1996). Developmental psychopathologists may be particularly well suited to study multifinal processes from an RDoC framework since RDoC constructs are transdiagnostic and can often be measured in early childhood. For example, preschoolers with high irritability at age 4 are more likely to be diagnosed with generalized anxiety and separation anxiety disorders (Wakschlag et al., 2015). Studying these multifinal processes using relevant RDoC-informed developmentally appropriate constructs may lead to improved understanding of when and how trajectories shift from normative to clinically concerning.

Developmental psychopathology researchers have long excelled at conceptualizing and measuring the contribution of environmental influences on equi- and multifinality. As with developmental processes, environmental influences are not well described in RDoC. The processes that give rise to psychiatric disorders are etiologically complex and involve biological and environment interactions across time and levels of analysis. However, the utility of adding an “environment” matrix to RDoC has been called into question at the risk of oversimplifying these complex phenomena (Beauchaine & Hinshaw, 2020). Instead, researchers could develop RDoC-informed models that address developmental and environmental processes specific to traits known to give rise to psychopathology (Beauchaine & Hinshaw, 2020). After all, biological markers of disease are rarely synonymous with expression of that disorder. In many instances Biology \times Environment interactions account for a greater proportion of variance in an outcome than the main effect in isolation (Beauchaine, Klein, Crowell, Derbidge, & Gatzke-Kopp, 2009). For example, in this special issue Liu and colleagues find that maternal symptoms of depression interact with infant high

cortisol area under the curve to predict elevated symptoms of psychopathology 6 months later (Liu et al., this issue). Thus, developmental psychopathologists could make a major contribution to our understanding of how these complex multifinal risk trajectories influence and are influenced by environmental exposures.

Identification of Multilevel Mechanisms Implicated in the Development of Transdiagnostic Vulnerabilities May Reveal Causal Pathways

In addition to improved measurement of multilevel equi- and multifinal developmental processes, developmental psychopathologists can contribute to the RDoC agenda by measuring the mechanisms by which early expression of vulnerable RDoC constructs are related to more fixed psychopathology later in life. Developmental researchers excel at identifying whether putative biological mechanisms are predictors, correlates, markers, and/or consequences of psychopathology (Sroufe, 2009), also termed “intermediate psychological constructs” by Kozak and Cuthbert (Kozak & Cuthbert, 2016). For example, in this issue Bush and colleagues demonstrate that a latent physiological profile comprising low resting respiratory sinus arrhythmia and elevated heart rate was predicted by early life stress and predicts poorer executive functioning in early childhood (Bush et al., this issue). Developmental psychopathologists can make important contributions to the study of etiopathophysiology of psychopathology because they have strong methods for examining vulnerability and risk factors that emerge before the expression of disorder.

Identification of a neurological mechanism is not equal to discovery of a biological cause of disorder. In other words, we should not “confuse biological mediation (the brain) with biological etiology” (Lilienfeld, 2014). Developmental studies may illuminate whether early exposures lead to changes in the brain that make some children more vulnerable to psychopathology, or whether some children are born with these brain-based vulnerabilities. For example, in this special issue Beauchaine and colleagues show that for boys with high internalizing symptoms, more externalizing behavior is related to lower anterior cingulate cortex volumes (Beauchaine et al., this issue). Yet the “cause” of these symptoms may not be the anterior cingulate cortex. In another example from this issue, high exposure to racial discrimination is related to low working memory, which in turn predicts psychosis. However, the “cause” of psychosis is not low working memory, it may not even be exposure to racial discrimination but that exposure is clearly a risk factor (Vargas & Mittal, this issue).

If we are to make improvements in our identification of causal mechanisms it is essential that these mechanisms be validated in diverse samples. Putative mechanisms that operate in one racial or ethnic group may not function in the same way in another (Gatzke-Kopp, 2016). For example, blunted cortisol responses to stress mediated the effect of early life stress on psychopathology in African American adolescents, but not their European American counterparts (Conradt et al., 2014). Reducing health disparities in psychopathology warrants inclusion of diverse racial and ethnic groups to ensure that interventions do not take a “one size fits all” approach by assuming that the pathways leading to psychopathology in a dominant racial group operate similarly for children who have been understudied in psychological research.

Developmental psychopathology researchers may come closer to identifying causal mechanisms through intervention research (Davis, Hankin, Swales, & Hoffman, 2018; Mackiewicz Seghete

et al., 2020). By including putative biological mechanisms in intervention design (Cicchetti & Gunnar, 2008), researchers can determine if their intervention targets change the biological mechanism of interest (Fisher, Gunnar, Dozier, Bruce, & Pears, 2006). For example, research with children who have been maltreated (Cicchetti, Rogosch, Toth, & Sturge-Apple, 2011), in foster care (Fisher et al., 2006), and children with child protective services involvement (Bernard, Hostinar, & Dozier, 2015) has shown that early intervention leads to typical regulation of the neuroendocrine system. This important research allows us to move beyond descriptive studies of how a predictor is related to an outcome, either concurrently or even prospectively, to consider mechanism of effect in human studies.

Conclusions

In the 1980s, Cicchetti described how clinicians and academicians rarely interact, which spawned the new field of development and psychopathology. RDoC in many ways is another iteration of this mutually informative process – a way for basic scientists studying psychopathology to produce rigorous and reproducible research that will lead to improvements in early identification, prevention, and treatment of mental illness. As others also have articulated, we believe developmental psychopathologists will be critical in these important efforts, and in many ways, the roots of RDoC were firmly planted decades prior by developmental psychopathologists (Achenbach, 1966; Cicchetti, 1984). In this editorial, we highlighted how the early origins of developmental psychopathology included RDoC principles before the RDoC framework was developed. We described here three important ways in which developmental psychopathology and RDoC can mutually inform one another.

In this special issue, we aim to broaden our understanding of how RDoC approaches can be leveraged to better understand the mechanisms and processes implicated in the development of psychopathology. We provide examples of studies in this special issue that exemplify how development and psychopathology conceptualizations can improve upon the existing RDoC framework. Studies in this issue are diverse and identify transdiagnostic symptoms (like sleep), transdiagnostic risk factors (like maternal hostility and racial discrimination), applications of RDoC to parents, and markers, mechanisms, and processes of risk before the expression of the disorder is apparent (Brown et al., this issue; Humphreys et al., this issue; Karalunas et al., this issue; Ostlund et al., this issue; Vargas et al., this issue). We believe that research presented in this special issue generates novel research questions espoused by development and psychopathology researchers to advance the developmental science of RDoC.

Funding Statement. This manuscript was supported by the National Institute of Mental Health under the following awards: R21MH109777 (to S.C. and E.C.), R01MH119070 (to S.C. and E.C.), and T32MH015755-39 (to D.C.). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute of Mental Health or the National Institutes of Health.

Conflicts of Interest. None.

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