June 21, 2019

Dear Dr. Murphy,

The Federation of Associations in Behavioral and Brain Sciences appreciates the opportunity to provide input as NIMH works to incorporate development and environment into the RDoC initiative.

FABBS represents 23 scientific societies and 60 university departments whose scientific members and faculty share a commitment to advancing knowledge in the sciences of mind, brain, and behavior.

FABBS recognizes the potential of RDoC to address the limitations of categorical, symptom-based psychiatric diagnoses. In order to achieve this goal, development and environment are crucial additions to the conceptualized RDoC matrix. We applaud your inclusive process and continued evolution of RDoC. As indicated in the Request for Comment, understanding and measuring development and environment is essential to promoting mental health and addressing illness. We support the consideration of development as a third dimension in the existing matrix. The units of analysis in the current matrix- -other than genes - are generally descriptive whereas the combination of genes and environment would widely be considered causal when thinking about development. With this important addition, RDoC can move beyond descriptions of the processes that underlie and sustain current cognitive, emotional, and behavioral functioning, to begin to address the origins, or causes, of these processes and thereby the domains of functioning incorporated in the RDoC.

To further support your inclusion of development and environment in RDoC, we offer specific examples from FABBS scientists. It has become increasingly clear that early environmental risk factors are associated with risk for a range of adverse physical and mental health outcomes during development. Some examples include prenatal risk factors such as maternal stress and infection and early life adversity such as trauma and stress, all of which have been associated with a variety of psychological disorders including depression, autism, schizophrenia, eating disorders, and anxiety disorders as well as with poor health outcomes such as diabetes. Given these findings, it is likely that environmental risk factors are more tightly connected to specific RDoC mechanisms and phenotypes than previously recognized.
1. **Ideas for how best to communicate the potential role of development and environment in RDoC-informed research.**

The mental health of individuals is strongly affected by their development and environment over time. Environmental risk factors interact with the shared phenotypes between disorders, and are likely more proximal to risk factors for the disorders than the disorders themselves. Development is the trajectory of an organism in a context and that context – or environment – can alter development. Adding development and environment gets to the heart of the stated goals of RDoC. How can NIMH address mental illness without understanding what accounts to the trajectory of the organism and the environment that shapes it?

When analyzing the importance of development, variation in the timing of maturational events has been found to correlate with mental health issues. For example, research examining pubertal timing effects on psychopathology has emphasized that a subset of adolescent females, those who experience early pubertal maturation relative to their peers, appear to be at increased risk for psychopathology. As another example, Dr. Thomas Olino of Temple University has proposed, in the context of development, that patterns of development (i.e., slower development of reward sensitivity), rather than absolute reward sensitivity, is a key factor in developing depression. In addition to the chronological timing of development, a consideration of the duration of development time may also shed light on questions pertaining to adaptive and maladaptive emotional, cognitive, and behavioral processes.

In short, a challenge to communicating the role of development and environment within the RDoC-informed research is the static nature of the matrix and the consideration of development and environment over time.

2. **Avenues that have proved useful for investigators to incorporate developmental trajectories and interaction with the environment into RDoC-informed research. Examples of RDoC-informed studies that investigate the impact of the environment or development on mental illness are particularly welcome.**

There are several important large cohort studies that have investigated how environmental risk factors impact mental health outcomes, including RDoC-informed constructs.

Some examples of these studies include:
• Adolescent Brain Cognitive Development Study (ABCD)
• Philadelphia Neurodevelopmental Cohort (PNC)
• Child Health and Development Studies (CHDS); and a soon to be funded follow-up of this cohort using an RDoC Framework entitled the “CHDS Healthy Brains Project,” PI Lauren Ellman
• Center for the Health Assessment of Mothers and Children of Salinas-CHAMACOS- a study focusing on exposure to pesticides and offspring development, and a variety of studies examining toxicant exposures during pregnancy on offspring development.

These and other longitudinal cohort studies have conducted involve following large, representative samples across development with quantitative measures of mental health, cognition, and/or brain structure/functions over time. However, there is considerable variability in how studies collect environmental exposure data, affecting the usefulness of those data. Interestingly, physical addresses have proven to be valuable in a variety of studies that have examined exposure to pollution, crime rates, and other neighborhood level factors across development. Finally, a variety of newer studies have begun collecting more detailed information about the family environment, nutrition, and breast feeding. Still, few studies have long-term follow-up data.

3. Gaps or means to expand opportunities for developmental and environmental research informed by RDoC.

The inclusion of development and environment in the RDoC matrix provides the opportunity to include detailed information about a number of important contextual and individual-level variables that likely influence how environmental risk factors impact developmental outcomes. For example, familial variables (e.g., parenting styles), cultural context, peer relationships, interactions with educators, information about child nutrition/breast feeding, level of physical activity, sleep, and genetic information (at the level of family history and/or polygenetic risk scores).

There are several existing gaps in the current RDoC matrix. For example, in the “acute threat” construct within the negative valence systems, there is no mention of observable human/child behaviors prominent in Kagan’s definition of behavioral inhibition. In addition, as we have already argued, the organization of the RDoC constructs is structured in a static manner. However, the empirical support for the structure is absent. In a developmental context, the organization of the constructs may differ or change over time. This is true for the organization within a domain, as well as across domains.

Empirically, there are currently few studies with repeated neuroimaging data across development (including early development) and assessment of RDoC constructs, which are vital for understanding how environmental
exposures influence brain networks associated with RDoC constructs. Similarly, few studies have included theory informed assessment of cognitive data (i.e., based on proposed mechanisms of exposures versus convenience of the assessment).

While in full support of the inclusion of development and environment, we feel obligated to voice an area of concern regarding RDoC. We are enthusiastic about the potential of RDoC yet recommend that it serve as an opportunity and not a limitation. As NIMH continues to build and improve upon RDoC we recommend that compliance with the RDoC structure maintain some flexibility. FABBS sees a risk to insisting on a set framework, particularly one that is still under construction.

Thank you for the opportunity to comment and appreciate your consideration. Please call upon FABBS as a resource.

Sincerely,

Juliane Baron
Executive Director