

Developing a Motor Systems Domain for the NIMH RDoC Program

Marjorie A. Garvey*¹ and Bruce N. Cuthbert²

¹Division of Translational Research, National Institutes of Mental Health, National Institutes of Health, DHHS, Rockville, MD;
²RDoC Unit, National Institute of Mental Health, Bethesda, MD

*To whom correspondence should be addressed; Division of Translational Research, National Institutes of Mental Health, National Institutes of Health, DHHS, 6001 Executive Blvd, NSC 9617, Room 7175, Rockville, MD 20852, US; tel: 301-443-4491, fax: 301-480-4415, e-mail: garvey@nhi.gov

During the last century, many studies have provided evidence that motor dysfunction is an important feature of neuropsychiatric disorders. Despite this, it is a relatively neglected area in mental illness research today. The extensive review of motor abnormalities in psychiatric illnesses by Peralta and Cuesta¹ in this issue provides some clues as to why this may be the case. These include the fact that there are many different tools which are used to detect motor signs, and not all of them assess the same signs (supplementary tables S2 and S3). In addition, particular motor syndromes, such as catatonia, may be under-recognized in mental illnesses other than schizophrenia (eg, mood disorders, autism spectrum disorders).

The review carefully examines the evidence for motor abnormalities in schizophrenia, mood disorders, obsessive compulsive disorders, autism spectrum disorders, and Alzheimer's disease. The authors provide compelling evidence that motor abnormalities are not epiphenomena of mental illnesses; they appear to be intrinsically linked to those disease processes that give rise to the cognitive, emotion regulation, and social deficits which are trademarks of these mental disorders.

In addition, motor abnormalities seem to be related to similar phenomena across different disorders. They are closely associated with cognitive impairments, appear to track disease burden, and may predict disease progression. In addition, as Schiffman's² commentary indicates, many years of retrospective and prospective empirical research provide compelling evidence that motor abnormalities may be an important predictive neurodevelopmental biomarker for psychosis.

Motor abnormalities can help separate out subgroups within the same DSM disorder (cf. the greater severity and worse prognosis of non-schizophrenic/non-affective psychoses when associated with catatonia). None of this should be surprising. Given the parallel, modular organization of frontal-subcortical systems, the physiologic (including neurotransmitter) and computational

differences contributing to dysfunction within higher-order circuits may also be present within the motor system. As noted in the commentary by Mittal et al,³ cognitive and motor functions are controlled by both the basal ganglia and cerebellar-subcortical circuits, and these 2 circuits work in concert with each other. In addition, cortical regions implicated in cognitive, social, and affective functions exert top-down modulatory effects on cortical and subcortical regions implicated in motor function. Thus the study of motor behaviors and their change over time, or in response to treatment, may eventually provide sensitive indicators of changes in cognitive and emotional regulation systems.

There are clear advantages to examining the motor system in psychiatric disorders as a window into cognitive and emotion regulation processes. Motor processes are overtly observable and highly reproducible between laboratory sessions and across multiple settings. They can be readily probed using a range of techniques, including detailed computational analysis of limb and eye movements, direct response to brain stimulation (TMS, tDCS, and related methods), and neuroimaging.

Overall, the review and commentaries make clear that the time is now ripe to study motor processes in mental illness and the authors suggest that, given the ubiquitous nature of motor abnormalities in mental illnesses, an approach based upon the NIMH Research Domain Criteria (RDoC) framework may be the best way to start. Similarly, an RDoC perspective to studying the link between motor processes and manifestations of cognitive/emotion regulation processes was the subject of an editorial in *Brain*.⁴ Such an approach would provide key insights into the relationship between motor and cognitive dysfunctions, and in particular, the associations between dysfunction in a specific motor circuit and behavioral abnormalities.

The need for an RDoC approach to the study of motor systems was put forward by experts taking part in the

2011 RDoC Cognitive Processes workshop. The NIMH RDoC workgroup requested further input from these individuals as well as others with expertise in motor systems. Their input made it clear that including an RDoC approach to the study of motor systems would bring critical insights into psychopathology.

Recently, a workgroup of the National Advisory Mental Health Council (NAMHC) was formed to oversee changes to the RDoC matrix. The charge to this workgroup is to oversee all changes in the RDoC matrix going forward. Changes can be proposed by scientists in the field, as well as by members of either the NAMHC workgroup or the NIMH RDoC workgroup. Additions, deletions, or edits regarding particular RDoC constructs will be evaluated via email and/or videoconferencing by a group of ad hoc scientists who are nominated by NIMH program staff, the Council workgroup members, and other scientists. Comments from the ad hoc group regarding the proposed changes will be considered by the NAMHC workgroup as well as by the NIMH RDoC workgroup, and implemented if all groups reach consensus.

The same process will be followed in vetting proposals for a new domain, a major new construct, or a new conceptual approach (eg, introducing a new organizing approach for the matrix, such as connectomics). However, for such significant changes an in-person workshop will be organized along the lines of the previous RDoC pattern (30–40 scientists meeting for 2–3 days) to consider the changes and produce a report to the NAMHC workgroup.

The initial input from the experts in 2011 had recommended the addition of a Motor Systems Domain since the alternative—a motor systems construct within the Cognitive Systems Domain—might not fully encompass the types of motor dysfunctions associated with psychopathology (catatonia, overflow movements, hyperactivity, psychomotor retardation, etc.). Consistent with the process described above, a workshop was organized in late 2016 to gather input from a large group of scientists and clinicians with expertise in motor systems, mental illness, or a combination of both. As with preceding Domain

workshops, participants reached consensus on the constructs and their exact definitions, and selected the related matrix elements. The experts and the NIMH RDoC staff proceeded to complete a report, which is now under consideration by the NAMHC workgroup.

This workshop is a reflection of the increasing scientific interest in motor systems as related to mental health. While RDoC provides one paradigm for investigating motor functions in mental disorders, it is important to note that other approaches remain available to investigators, whether using traditional diagnostic categories or other procedures (eg, computationally determined clusters or dimensions) as the basis for research designs. In any case, the manuscripts in this special section provide clear evidence of the contemporary scientific basis for research in this area, and make a strong argument for renewed research and clinical attention to these systems. It is evident that recent advances in the understanding of motor systems and their relationships to other aspects of mental disorders, combined with new perspectives on diagnosis, demonstrate a strong potential to add to our knowledge about the mechanisms of psychopathology and the development of diagnostic and predictive biomarkers.

Acknowledgment

The authors have declared that there are no conflicts of interest in relation to the subject of this study.

References

1. Peralta V, Cuesta M. Motor abnormalities: from neurodevelopmental to neurodegenerative through “functional” (neuro) psychiatric disorders. *Schizophr Bull*.
2. Schiffman J. Motor issues in the clinical high risk phase of psychosis. *Schizophr Bull*.
3. Mittal V, Bernard J, Northoff G. What can different motor circuits tell us about psychosis? An RDoC perspective. *Schizophr Bull*.
4. Rowe J. Editorial. *Brain*. 2015;138:2461–2462.