Keeping an open attitude towards the RDoC project

MARIO MAJ

Department of Psychiatry, University of Naples SUN, Naples, Italy

In the 1970s, a programme was launched in the United States which had two objectives: a) to improve the reliability of psychiatric diagnoses under ordinary clinical conditions; b) to facilitate the elucidation of the pathophysiology of mental disorders. In order to pursue these different objectives, the same tool was regarded as appropriate: a diagnostic system based on operational criteria defining in an explicit and precise way the various mental disorders.

The first of the above objectives seems to have been achieved to some extent, although a conclusive research evidence, collected in ordinary clinical settings, is still lacking (1). The improved reliability of psychiatric diagnoses may have been attained, however, at the expense of an oversimplification of psychopathology (2) and a dehumanization of psychiatric practice (3). We may have lost part of the essence of some psychopathological constructs by translating them into operational terms, and we may have lost part of the essence of the psychiatric profession by reducing the diagnostic process to a check of the presence or absence of a series of symptoms.

The second of the above objectives has apparently not been achieved, as acknowledged by the leadership itself of the DSM-5 Task Force (4). In spite of four decades of intensive and costly research, the pathophysiology of mental disorders remains elusive. One could argue, however, that a bulk of neurobiological data has been indeed collected, and several models developed. The puzzle to be composed may be just much more complex than originally envisaged, and a declaration of failure may be actually premature.

If the programme has indeed failed to achieve its second objective, several interpretations are possible. The first, and the simplest, is that all mental disorders defined within the programme are not valid disease entities, i.e., the entire diagnostic system does not carve nature at its joints. The second is that, although some of those disorders may be valid disease entities, the level at which they have been described is higher than that at which meaningful pathophysiological correlates are likely to emerge, i.e., we need some intermediate entities on which to base our search for neurobiological mechanisms. The third is that absence of evidence should be regarded as evidence of absence, i.e., mental disorders may be not amenable to a pathophysiological explanation in the same sense as, say, cardiological or neurological diseases. Damage to the neural substrate may be not necessary for failure of psychological function (5,6) and/or a variety of higher-order processes may intervene between the level of neurobiological vulnerability and that of psychopathological manifestations, so that a bottom-up reductionistic approach becomes insufficient

(7). The nature of psychopathology may be intrinsically heterogeneous in this respect, with higher-order processes accounting for the identity of some mental disorders (e.g., anorexia nervosa) much more than they do for others.

The Research Domain Criteria (RDoC) project is in conceptual continuity with the programme launched in the 1970s. One of its objectives is, again, to facilitate the elucidation of the neurobiological underpinnings of psychopathology. The other is to generate a diagnostic system which is more valid than that produced by the previous programme, being based, in analogy with the rest of medicine, on biological measures. In order to pursue these different objectives, the same tool is regarded as appropriate: a research framework including some functional domains, each consisting of behavioral dimensions that have been at least preliminarily related to a particular brain circuit or area.

The outline of the RDoC proposed dimensions available on the National Institute of Mental Health website is indeed impressive. Contrary to what might be inferred from the reports published in scientific journals, those dimensions do not only include “observable behaviors”, but also constructs such as “perception and understanding of self” and “understanding [others’] mental states”, so that the “experiential” component of psychopathology is also represented. The list of neurobiological variables is probably overinclusive, so that the reader is unable to identify the most promising ones (would some indication of the level of evidence available for each item be useful?). A (short) list of references is provided at the end of each section, but these references are not keyed to the proposed variables. Overall, however, the framework is remarkably informative for researchers.

Nevertheless, the gap between the proposed dimensions and the signs and symptoms that, as Cuthbert acknowledges, are “the actual clinical phenomena that bring patients to the clinic” (8) is sensible in several areas. If the problem with the DSM categories may be that they are too distant from the level of neuroscience, the problem with at least some of the RDoC constructs may be that they are somewhat distant from the level of clinical phenomena. Cuthbert seems to be confident that “sooner or later” it will be possible to explain even complex symptoms, such as delusions, “in terms of dysregulation in basic brain operations” (8). What happens, however, if some of those symptoms are found not to be explainable in neurobiological terms? Will they follow the fate of current diagnostic categories in being regarded as “invalid” constructs? Indeed, the RDoC project may be seen by some scholars as a

further step, after the introduction of operational diagnostic criteria, in the oversimplification of psychopathology and dehumanization of psychiatric practice. The concern may be raised that we are gradually departing from the essence of psychopathology rather than approaching it, and that we are further downgrading the humanistic component of the psychiatric profession just at a moment in which this component is being re-evaluated in the rest of medicine.

An alternative perspective, however, is that the RDoC project may represent a stimulus to a reconceptualization of some complex symptoms. Indeed, several elements of the current definition of delusions (i.e., that they represent “false beliefs”, that they are based on an “incorrect inference”, and that such an inference always regards “external reality”) have been recently questioned, at least in the case of schizophrenia (9). What can be explained in neurobiological terms may not be the patient’s metaphorical utterances, but the basic pathological experiences that the patient tries to convey through those utterances. A more in-depth exploration of those experiences may be therefore warranted.

The behavioral (and experiential) dimensions proposed by the RDoC project are expected to “cut across traditional diagnostic entities” (8). These latter entities would therefore be, in Jaspers’ terms, “mosaic-like structures” consisting of the same recurring elements. This remains, however, a hypothesis. At least some of those dimensions may be found to have different nuances and neurobiological correlates in partial or full relationship to current diagnostic constructs. Hopefully, research designs within the project will allow distinguishing between these alternative possibilities. Cuthbert’s argument that analyses “could be conducted in terms of the DSM factor, the RDoC dimension, and the interaction” (8) seems to point in this direction.

The RDoC project is stated to “depart markedly from the DSM and ICD processes”, which were based on “extensive workgroup meetings” that “generated the sets of diagnoses” (8). One could argue, however, that the RDoC functional domains and the dimensions included in each domain have been identified through a similar process. They are at present the result of a consensus among experts. Of course, that consensus was based on the available research evidence and is going to be reconsidered throughout the process, but we should not forget that the same applies to current DSM and ICD constructs, several of which have been the subject of many hundreds of studies and have been repeatedly reconsidered and revised along the years on the basis of research evidence. Incidentally, an important feature of DSM and ICD workgroups has always been their international composition, while a recurring complaint has been that practicing clinicians, who might provide a useful viewpoint about the applicability of the proposed system under ordinary clinical conditions, were not sufficiently represented. It may be perhaps advisable to reflect upon this.

Overall, the RDoC project seems much more likely to achieve to some extent, in the foreseeable future, its first objective (i.e., to facilitate the elucidation of the neurobiological underpinnings of psychopathology), than the second, at least as currently formulated (i.e., to generate a diagnostic system “based upon neuroscience and behavioral science rather than descriptive phenomenology”). Achieving this latter objective, in fact, would require developing a set of behavioral and biological measures whose test-retest/inter-operator reliability as well as sensitivity/specificity in predicting outcomes (including response to various treatments) is at least the same as that of current symptom-based measures, and whose assessment is feasible and cost-effective in a reasonable range of clinical settings worldwide. Most likely, something not attainable even in the long term. It would be probably wise, therefore, to refrain from a polemic confrontation with the DSM and ICD which is unwarranted, disruptive to the field, and confusing to patients and families, to colleagues of other medical disciplines, to policy makers and to the public opinion.

It may also be appropriate to lay a greater emphasis on the less ambitious version of the second objective, which also appears in Cuthbert’s paper, i.e., the development of neurobiological measures which may help in *subtyping* rather than *replacing* current diagnostic entities, in order to improve prediction of outcome and treatment response. As stated in a recent paper of which T. Insel was a co-author (10), “the real opportunity for psychiatry is to use the emerging advances in genetics, molecular biology, imaging and cognitive science to supplement, rather than replace, the symptom-driven diagnosis”.

On the other hand, in consideration of all the above, it is probably advisable for all scholars to keep an open attitude towards the RDoC project. By interfacing more directly with the level of neuroscience, this project is likely to usefully complement the current diagnostic systems, which interface more directly with the level of clinical reality. Developing cross-walks between the two approaches, in a climate of reciprocal respect, is an endeavor that can only enrich psychiatry and related disciplines and increase their credibility.

References

1. Westen D. Prototype diagnosis of psychiatric syndromes. *World Psychiatry* 2012;11:16-21.
2. Parnas J. The Breivik case and “*conditio psychiatrica*”. *World Psychiatry* 2013;12:22-3.
3. Andreasen N. DSM and the death of phenomenology in America: an example of unintended consequences. *Schizophr Bull* 2007; 33:108-12.
4. Kupfer DJ, First MB, Regier DE. Introduction. In: Kupfer DJ, First MB, Regier DE (eds). *A research agenda for DSM-V*. Washington: American Psychiatric Association, 2002:xv-xxiii.
5. Bolton D. *What is mental disorder? An essay in philosophy, science, and values*. Oxford: Oxford University Press, 2008.

6. Maj M. Mental disorders as “brain diseases” and Jaspers’ legacy. *World Psychiatry* 2013;12:1-3.
7. Kendler KS. Toward a philosophical structure for psychiatry. *Am J Psychiatry* 2005;162:433-40.
8. Cuthbert BN. The RDoC framework: facilitating transition from ICD/DSM to dimensional approaches that integrate neuroscience and psychopathology. *World Psychiatry* 2014;13:28-35.
9. Maj M. Karl Jaspers and the genesis of delusions in schizophrenia. *Schizophr Bull* 2013;39:242-3.
10. Kapur S, Phillips AG, Insel TR. Why has it taken so long for biological psychiatry to develop clinical tests and what to do about it? *Mol Psychiatry* 2012;17:1174-9.

DOI 10.1002/wps.20111