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Anticipating *DSM-V*: Opportunities and Challenges for Cognition and Psychosis

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Cognition and Psychosis: Opportunities and Challenges for the Future of Psychiatry

As outlined by the Bora[1] article and commentary included in this issue of *Schizophrenia Bulletin*, the field has seen an increasing emphasis on the importance of cognition in understanding psychosis over the past 20 years. There is ample evidence that a large percentage of individuals with schizophrenia suffer from impairments in a range of cognitive domains, eg, Reichenberg et al,[2] and growing evidence that the level of cognitive impairment predicts functional abilities in schizophrenia (social, occupational, and living status), eg, Heinrichs et al,[3] Cervellione et al,[4] McClure et al,[5] and Green et al.[6] As such, the hope is that by improving cognitive function among individuals with schizophrenia, we may be able to improve functional outcome in this very debilitating illness and thus improve the quality of life for individuals with schizophrenia and address important public health and humanitarian concerns. However, as noted by Bora and others,[7] the question of how to incorporate conceptions of cognitive impairment into existing diagnostic criteria for schizophrenia and/or other psychotic disorders raises a challenging set of issues. Here, we outline what we think are some of the key issues in this regard and some potential pathways to address these challenges.

Should Cognitive Function Be Included as One of the Diagnostic Criteria for Schizophrenia?

One obvious way in which to highlight the importance of cognitive function for understanding schizophrenia would be to include cognitive dysfunction as one of the diagnostic criteria for schizophrenia. However, as noted by Bora and others,[7] including cognitive dysfunction as one of the "criterion A" symptoms for schizophrenia in the *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) (*DSM-V*) would be problematic from a differential diagnosis viewpoint. A critical question in this regard is whether cognitive impairment as currently determined will facilitate the specificity and/or positive predictive power in identifying those individuals with schizophrenia. As discussed by Bora in this issue and previously by one of us,[8,9] current cognitive methods are unlikely to create a sufficient "point of rarity" with other disorders that would be the sole justification for the inclusion of a cognitive criterion in the diagnosis of schizophrenia. Recent meta-analyses and reviews have demonstrated that the profile of cognitive impairment is similar across schizophrenia, schizoaffective disorder, psychotic bipolar disorder, and even psychotic major depression, though the level of impairment is greater in schizophrenia.[10–18] As such, it is highly unlikely that cross-sectional assessments of cognitive function alone would allow us to distinguish between an individual who has schizophrenia vs someone with another psychotic disorder. However, it is noteworthy that the great difficulty in distinguishing negative symptoms such as amotivation, apathy, and anhedonia in schizophrenia from similar symptoms and signs in depression did not preclude their inclusion as a criterion in previous versions of *DSM*.

Does the relatively weak capacity of cognitive impairment to separate schizophrenia from other illnesses suggest that it has no potential utility as a diagnostic indicator? That is doubtful. While cross-sectional assessments of psychosis and cognition may have weak diagnostic discriminating power, characterizing the longitudinal course of cognitive function may have more utility as a diagnostic tool. Cognitive dysfunction in individuals with schizophrenia has been demonstrated to be more stable and less dependent on symptom severity[19–21] than cognitive dysfunction in individuals with other psychotic disorders.[12] Furthermore, in many individuals who develop schizophrenia, cognitive impairments occur very early in life and often precede the onset of any clear clinical indicators of psychosis.[22,23] However, as noted by Bora and others, there is as of

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yet very little data that prospectively address this hypothesis and growing evidence that at least some residual cognitive impairment may remain between episodes in affective psychoses.[2,24–26] Thus, the question of whether longitudinal assessments of cognitive function have more predictive utility awaits further research that prospectively compares the stability of cognitive function across psychotic disorders at different stages of illness. Of course, should research in this domain suggest that the longitudinal course of cognitive function has more predictive utility, it will raise important practical issues as to how to actually implement such longitudinal assessments in the fields of psychiatry and psychology, which are largely overburdened and under funded in the world's current health-care systems.

Is It Still Important to Include Assessment of Cognition in *DSM-V*, Even if not Used as a Diagnostic Criterion?

Diagnostic tools such as the *DSM* system are mostly frequently thought of as tools for differentiating among individuals with different psychiatric disorders. However, the greatest purpose of diagnostic assessment tools is for identifying "treatment-relevant" phenomena (which may or may not have diagnostic specificity), thereby improving treatment for our patients. This may be the most important reason to include an assessment of cognition in schizophrenia in the *DSM-V*. As noted above, a large body of evidence suggests that cognitive function constrains functional outcome in schizophrenia.[3,4,27–29] However, we also know that cognitive deficits are not well treated by current antipsychotic medications,[30] and thus, it is important to highlight the potential need for additional treatments specifically targeting cognitive impairment in schizophrenia and other psychotic disorders.[31,32] Including cognitive dysfunction as a treatment-relevant dimension in the *DSM-V* would help serve this purpose. Such treatments may be pharmacological or behavioral[33–35] as both avenues hold promise as potential pathways by which to enhance cognition and functional outcome in this illness. Furthermore, the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) group and the Food and Drug Administration have already worked together to build consensus on clinical trial designs that could support an efficacy claim for enhancing cognition in individuals with schizophrenia.[36] If safe and effective treatments become available for patients with schizophrenia, it will be very important for clinicians to be aware of their importance.

How Should We Measure Cognition?

The suggestion that cognitive function should be included as a treatment-relevant dimension to be assessed in the *DSM-V* raises a vexing question: Exactly, how shall clinicians accomplish this goal? There are 2 separable components to this question. The first is how many different domains of cognition we need to assess in order to generate sufficient information about cognitive function in individuals. The second is the question of what tools, measures, or approaches clinicians should use to assess cognition. In an ideal world, a diagnostic evaluation of a patient with serious mental illness would include a comprehensive evaluation (or someday, perhaps, a diagnostically specific one!) by a neuropsychologist or other individual with specialized training in the assessment of cognition. Such a comprehensive evaluation would cover many domains of cognition and would provide separate indicators of function in each domain (eg, working memory, episodic memory, processing speed, etc). This is the approach taken in the MATRICS battery, which provides assessment of 7 putatively separable domains of cognitive function in schizophrenia.[37–39]

Although this may be the ideal, we know that the practical and economic constraints facing many clinics and treatment settings would render such a suggestion unfeasible. Thus, it is important to consider what other options may provide enough information to guide treatment planning. One important consideration is whether there are some measures available for use in schizophrenia that by themselves can account for a large amount of the variation captured by full neuropsychological assessment. The answer may very well be "yes." For example, work by Dickinson et al[40] has shown that impairments on digit symbol–type tasks have the largest effect sizes among many different measures for characterizing cognitive impairment in schizophrenia. Such tasks are interesting as they are of a class of "kitchen-sink"–type tasks that may elicit large deficits in schizophrenia because they tap into many different cognitive abilities simultaneously (eg, working memory, episodic memory, attention, processing speed, etc). Thus, such tasks may show large effect sizes in schizophrenia because they are influenced by impairments in many different cognitive domains, many (or all) of which may be impaired in the same individuals with schizophrenia. Thus, while such tasks may not be useful in some contexts (eg, identifying selective impairments, translation to animal models), they may have great utility in contexts where there is only time or resources to administer a small number of measures. In support of this suggestion, data acquired in the Clinical Antipsychotic Trials of Intervention Effectiveness study suggested that digit symbol performance accounted for 61% of the variance in the total cognitive scores derived from a large neuropsychological battery.[41] Such results suggest that when limited resources constrain the types of cognitive assessments that can be administered, careful selection of a small number of tasks that are strongly predictive of performance on full batteries may be a viable alternative that will provide useful information for treatment planning.

A second important consideration is whether it is necessary to use a formal assessment of cognition (eg, a cognitive or neuropsychological task), given that many clinicians will not have any experience in administering such measures. For example, there are some tools that have been developed that ask individuals to self-report on their level of cognitive function in one or more domains.[42–44] Such interview-based measures would in theory be easy for clinicians to administer as they would be similar in format and style to more traditional diagnostic assessments. However, there is growing evidence that self-reports alone do not provide sufficiently valid indicators of cognitive function[45] and that informant reports may be necessary in order to assess cognitive function validly in individuals with schizophrenia.[43,45] Nonetheless, there are enhanced versions of such interview-based assessments, currently being evaluated as part of the MATRICS Co-primary and Translation consortium, that may provide more valid assessments of cognitive function based on clinician-administered interviews that do not require formal cognitive testing.

Yet another option is to use what are referred to as assessments of functional capacity, such as the UCSD Performance-Based Skills Assessment.[46,47] These tools assess cognitive function in the context of performing what are thought to be ecological valid skills and tasks such as making phone calls, dealing with one's medicine, or reading maps. These measures have shown good utility in predicting functional outcome[43,46] and in some cases have been more strongly related to functional status than more traditional measures of cognitive function.[28] There are brief versions of such measures available,[48,49] and it is at least theoretically possible that a wide range of clinicians could learn to administer such measures reliably.

Should cognition Be Assessed for All Psychotic Disorders?

The relevance of cognition for understanding function has received the most attention in relation to schizophrenia. However, as described above, there is abundant evidence for cognitive impairment in a range of both affective and nonaffective psychotic disorders, suggesting that it is just as critical to assess cognition for these disorders as it is for schizophrenia. Furthermore, there is growing evidence that cognition is also relevant for understanding functional status and outcome in affective psychoses as well as nonaffective psychoses.[50–53] Such data suggest that cognitive function is a potentially critical treatment target in affective psychoses as well as in schizophrenia[54] and that assessments of cognition should also be considered as treatment-relevant dimensions for the characterization of individuals with bipolar disorder or psychotic major depression in the *DSM-V*. However, it has been clearly established that cognitive impairment in psychotic disorders is most severe in schizophrenia and that the time has come for the inclusion of cognitive impairment as a component of the diagnostic assessment of schizophrenia. As pharmacological or behavioral interventions that are effective for enhancing cognition become available, it will be important for clinicians to have a clear way of determining which individuals should be provided with such treatments and whether these treatments are effective in their patients.

Summary

The current debate regarding the role that cognitive function should play in the diagnostic criteria for schizophrenia in the *DSM-V* has been a healthy one that has engendered much useful discussion and potentially interesting pathways for future research. At this point, there is little support for the idea that cognition should be included as a criterion A–type symptom that would differentiate those individuals with schizophrenia from individuals with other psychiatric illnesses. However, there continues to be much interest in including assessments of cognition in the *DSM-V* as a means of highlighting the importance of cognitive function for understanding functional status and outcome and to facilitate attention to cognitive function in treatment planning. However, as discussed here and in the Bora commentary, these suggestions do raise important theoretical and practical challenges as to how to best accomplish these goals and to provide a means of assessment of cognition that is viable across a wide range of contexts. In order to accomplish these goals, the structure of *DSM-V* will need to be modified to facilitate the inclusion of treatment-relevant domains that may not be part of the diagnostic criteria such as including assessments of one more domains for all disorders (eg, suicidality and perhaps even cognition) or assessments of domains that may be specific to certain classes of disorders (eg, cognition for psychotic and mood disorders). Bora et al suggest either using specifiers to indicate which individuals with schizophrenia have cognitive impairment or using a dimensional assessment of cognition. We tend to favor a dimensional approach as one that preserves the most information and does not necessitate placing what may be arbitrary thresholds on the level of cognitive dysfunction that would be sufficient to warrant a specifier of cognitive impairment. Furthermore, it is becoming increasingly apparent from the work of Bora and others that cognition may also deserve attention in the assessment of individuals with affective as well as nonaffective psychosis, and thus, whatever approach is adopted in the *DSM-V* for assessing cognition in schizophrenia may also need to be applicable to individuals with other disorders as well. These are solvable challenges and well worth the effort in terms of their potential payoff for enhancing the quality of life of people with mental illnesses and reducing demands on public health resources.

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