Editorial: Unmet Therapeutic Needs

Modern pharmacotherapy for schizophrenia began with the introduction of chlorpromazine in 1952. About the same time principles from social psychiatry were being implemented, and the focus of care shifted away from chronic care hospitals. Empirically validated forms of psychosocial treatment have now joined drug treatment in evidence-based practice. But it has been difficult to robustly alter long-term outcome. Current treatments appear most robust in effecting psychosis, and there has been little progress on the aspects of schizophrenia that appear to account for poor functional outcomes. In this regard, impaired cognition and primary negative symptoms represent unmet therapeutic needs and challenge the field for innovation and discovery.

The National Institute of Mental Health (NIMH) has crystallized a focus on cognition in schizophrenia with the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) process and, in doing so, has facilitated a productive collaboration between industry and academic scientists and Food and Drug Administration (FDA) and NIMH leaders. Linda Brady, Wayne Fenton, and Ellen Stover have led the NIMH effort. Steve Marder as principal investigator (PI) and Michael Green as co-PI have provided wise leadership, and the products of the work have significantly advanced the field. A consensus view on the assessment of cognition as a treatment outcome measure was published in *Schizophrenia Research.* Test selection for the MATRICS Cognition Assessment Battery was constrained by the requirement of established psychometric properties and the limitation of the individual cognitive domain measures to well-established tests. This is a major step forward in determining what and how to measure when conducting a clinical trial to test efficacy for cognition. Commentaries on why progress in drug discovery has been slow for this disease were also provided. Identifying new cognitive neuroscience-based approaches to parsing and measuring cognitive processes was a central goal of this MATRICS meeting. Mark Geyer and Robert Heinssen organized the meeting and present the results as a theme in this issue. The guest editor’s introduction provides a guide to the several sources of information on MATRICS results.

In a companion theme for this issue, Phil Harvey provides a summary of the 2005 Mt. Sinai Conference and provides reports on the implementation of cognition-based treatments. The compilation of articles under this theme describes the effectiveness of cognitive remediation or other behavioral interventions, as well as predictors of good outcome of such therapies. The Mt. Sinai meetings, sometimes as a satellite to the International Congress on Schizophrenia Research, provide an annual gathering for scientists interested in schizophrenia cognition.

The next step involved negative symptoms as an unmet treatment need. The negative symptom concept and requirements for assessment and clinical trial design were considered at a January 2005 workshop at NIMH in which the FDA participated. A consensus view on the components of the negative symptom construct was developed, and a clinical assessment instrument is currently being produced. Brian Kirkpatrick will guest edit a report from this workshop with theme articles scheduled for the January 2006 issue. Other themes planned in 2006 include topics on remission and recovery, schizophrenia risk factors, cognitive deficits in at-risk subjects, ethics, and schizophrenia endophenotypes. We plan a theme issue on prodromal schizophrenia and early intervention for the January 2007 issue. In reviewing unsolicited manuscripts, we will be especially interested in high-quality data reports that advance knowledge related to these themes.

It is gratifying to see NIMH, FDA, industry, and academic scientists focused on these 2 core domains of psychopathology in schizophrenia. The realization that the refinement of present therapeutic approaches will not adequately address these challenges is critical. Investment of resources and creativity in new directions are needed to achieve innovative advances. “Me too” approaches need to give way to new therapeutic hypotheses and novel mechanisms if the unmet treatment needs in schizophrenia are to be addressed.
References