Conference Report: The Seventh Biennial Mt. Sinai Conference on Cognition in Schizophrenia

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The Seventh Biennial Mt. Sinai Conference on Cognition in Schizophrenia was held on April 1 (afternoon) and April 2, 2005, at the Savannah International Trade and Conference Center. As it has been since 1999, this meeting was held as an official satellite of the International Congress on Schizophrenia Research (ICOSR). This meeting was attended by 295 individuals, for at least part of the meeting, making it the largest stand-alone meeting addressing cognition in schizophrenia.

The themes of the oral presentations at the meeting were consistent with two major trends in cognition in schizophrenia: a focus on treatment of cognitive deficits and a comprehensive approach to understanding the causes and functional relevance of cognitive deficits. In addition to the two sessions of oral presentations by high-level scientists, there was also a poster session, which featured 54 presentations. Of these poster presentations, 18 were also presented at a special cosponsored session at the ICOSR.


This morning session was introduced by Peter Buckley, Medical College of Georgia, after welcoming remarks from Jack Gorman, MD, chair of the Department of Psychiatry at Mt. Sinai. This session focused on treatment of cognition in schizophrenia, based on the now well appreciated linkage between cognitive impairments and impairments in everyday life skills in people with schizophrenia. This session included discussions of novel pharmacological strategies, novel behavioral strategies, potential genetic mediators of treatment response, and several critical papers on conceptual and methodological issues. These included discussions of how best to measure cognition as an outcome in clinical trials, what additional aspects of outcome should be measured, what defines good treatment response, and what are the predictors of this response.

Michael Green and Keith Nuechterlein presented an interim report on the current status of the cognitive assessment battery that has been developed by the National Institute of Mental Health–funded Measurement and Treatment Initiative for Cognition in Schizophrenia (MATRICS). Presenting both the tests and the methods used to select them, Green and Nuechterlein showed the audience the systematic process that was used to select the consensus battery. As important, they made it clear that in addition to cognitive assessments, other measures of outcome would be included as well.

The next two presentations focused in detail on some of the conceptual and interpretative issues associated with the treatment of cognitive impairments. Richard Keefe presented a discussion of alternative measures of outcome, including performance-based measure of functional skills and the development and validation of interview-based methods to assess cognition and related functional skills deficits. Such measures are not only required for Food and Drug Administration (FDA) approval of new treatments for cognition, but they also provide information about the breadth of treatment response associated with treatment. Robert Bilder presented an evaluation of how improvement is defined in treatment studies, including discussions of what would constitute a clinically meaningful effect and how “normalization” of performance would be defined. These are important issues, in that patients with schizophrenia have substantial cognitive limitations, and it is entirely possible that patients could manifest improvement in their cognitive functioning that would not have any substantial potential for real benefit.

Cognitive impairments are also present in the schizophrenia spectrum and may be determined by some of the same biological factors as schizophrenia. Larry Siever presented information about treatment with noradrenergic (NE) and dopaminergic (DA) compounds, showing that both pergolide and guanfacine had beneficial, but apparently distinct, effects on cognitive impairments in schizotypal personality disorder (SPD). Both treatments enhanced context processing and other indices of executive working memory, and NE manipulations improved...
spatial, but not verbal, working memory in patients with SPD. Frank Bymaster’s presentation, also focusing on pharmacological interventions, presented important basic science data on the NE transporter and its role in cognition. As the NE and DA transporters interact in the cortex, interventions that block the NE transporter have the potential to increase DA functioning. Increasing dopaminergic tone in the cortex has been hypothesized to improve cognitive functioning, and thus manipulations of the NE transporter may be important cognitive enhancers. Directly relevant to this issue, Terry Goldberg showed that genetic factors have notable impacts on treatment response. Alternations in the catechol-O-methyltransferase (COMT) genotype have been shown to influence both cognitive and negative symptom responses to treatment with atypical antipsychotic medications. Further, genotypic factors also interact with the effects of tolcapone, a drug that directly influences COMT activity. Thus, genetic factors might influence the extent to which treatments that increase regional cortical activation of various neurotransmitters have a truly beneficial effect.

The final two presentations were not aimed at neurotransmission but rather at the potential of other pharmacological and behavioral interventions to improve cognition in schizophrenia. Craig Smith presented data on an experimental treatment, HP-184, which increases the integrity of white matter tracts in experimental models of spinal cord injury. Since white matter abnormalities may be present in schizophrenia, treatments that increase white matter density and integrity may have beneficial cognitive effects. This treatment should have promise as well in treatment of other conditions that affect white matter integrity. Finally, Alice Medalia presented information regarding the successful cognitive remediation of patients with schizophrenia. In contrast to previous efforts, these newer interventions have produced larger and more persistent benefits, as well as more generalizable effects. Predictors of better response are both the intensity of the intervention and the dose of treatments received. Thus, there is a rationally understandable relationship between treatment integrity and outcomes.

Memory in Schizophrenia: From Genes to Jobs

This afternoon session focused on memory impairments, broadly defined, and presented information ranging from the genetic determinants of cognition to treatment with specialized behavioral techniques. Daniel Weinberger presented information on several different genetic factors that may be relevant to schizophrenia and memory in specific. The Brain Derived Neurotrophic Factor (BDNF) genotype appears extremely promising in this regard. In normal individuals, variation in the BDNF genotype predicts anatomy of the hippocampus, which, in conjunction with data suggesting that normal memory is influenced by the genotype, suggests a possible convergent mechanism for both findings of episodic memory deficit and hippocampal abnormalities in schizophrenia. Joseph Friedman presented data relevant to cortical organization and cognitive functioning. Demonstrating that disorganization and cognitive functioning. Demonstrating that disorganization in the arrangement of cortical white matter (i.e., reductions in “fractional anistropy”) was common in schizophrenia, Friedman also showed that these white matter abnormalities were correlated with both real world functional outcomes (independent living status) and performance on tests of processing speed and working memory.

Memory impairments are present across the course of the illness and may define meaningful subgroups of patients. Larry Seidman presented data regarding the relative severity of memory impairments prior to the onset of psychosis. In contrast to executive functioning indices, measures of episodic memory manifest considerable impairment prior to the onset of psychosis and may constitute markers of vulnerability to the condition. Similarly, Bruce Wexler reported that differences in patterns of memory impairment and distributions of gray and white matter defined distinct subgroups of patients with schizophrenia. Specifically, white matter abnormalities were associated with episodic memory impairments. Further, he addressed a number of issues associated with global cognitive impairments and their implications for the disturbances in white versus gray matter in the brain in schizophrenia. Scott Sponheim examined evoked potential (EP) correlates of implicit and explicit memory processes in schizophrenia patients and their relatives. Relatives of patients with schizophrenia shared impaired explicit memory and spared recognition memory. EP evidence suggested that impaired explicit memory was associated with abnormalities in the processing of the information that could not be related only to the input of the material.

While memory deficits are prominent in schizophrenia, affective impairments are very salient as well. Ruben Gur presented information to demonstrate that memory for affective stimuli was impaired, in a manner similar to episodic memory for verbal stimuli. Much like verbal memory, there is evidence of impaired processing of affective stimuli at the time of encoding, accompanied by patterns of abnormal activation, much like previous reports of abnormal patterns of brain activation during verbal learning. Judith Jaeger presented data suggesting that patients with different profiles of cognitive impairments could be identified and discriminated. These subgroups were then related to variations in their functional outcome, validating the subdivision of the subjects on the basis of greater or lesser degrees of cognitive abnormalities.

Two other presentations addressed the important issue of whether cognitive enhancement leads to improvements in functional outcomes. This is an important topic and the tie-in to the “jobs” part of “genes to jobs.” Kim
Mueser and Susan McGurk presented the results of an effectiveness study of cognitive enhancement added onto a structured employment placement program. Their findings were that the cognitive remediation interventions, delivered in a computerized format, led to a statistically significant benefit compared to the employment intervention alone. In a similar presentation two randomized clinical trials were presented by Morris Bell, who reported that a similar cognitive remediation intervention led to improvements in patients randomized to receive this treatment in addition to supportive employment interventions. Most important, the effects of this intervention were persistent after the intervention itself terminated.

The data presented in the oral presentation sessions at the Mt. Sinai conference highlight the sophistication and success associated with research on cognition in schizophrenia. The diversity of this research was also evident at the poster sessions. While reviewing all the posters is clearly beyond the scope of this brief conference report, there were several different themes evident. There were 12 posters on cognitive enhancement, equally divided between pharmacological and behavioral interventions, and an additional 5 posters on basic pharmacology relevant to schizophrenia. Three posters focused on genetic factors, including COMT and BDNF. There was a large selection of presentations on psychophysiology, including EP and sensory gating studies. The topic of the imaging correlates of memory performance was well represented, as were studies of the factory structure and correlates of impaired cognition. Multiple posters were also presented on prodromal and first episode patients, as well as a selection of posters on aging and late life phenomena. Finally, several different posters examined enhancements in cognitive and functional assessments of the illness, with an eye toward developing valid and portable assessments of cognitive and functional impairments suitable for use in clinical trials.

**Summary**

This meeting reflected both the interest in and diversity of research on cognition in schizophrenia. The meeting was as international as the international congress, with posters originating from 10 different countries and attendees from at least 8 more. It is our plan to continue, and the next meeting of the ICOSR, in Colorado Springs, Colo, in 2007 will also have a cognition satellite meeting. If you are not on our mailing list, you can be placed on it by sending an e-mail to cognition2007@cs.com.