

Social Cognition in Schizophrenia: Recommendations from the Measurement and Treatment Research to Improve Cognition in Schizophrenia New Approaches Conference

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This article summarizes the discussion from a breakout group at the National Institute of Mental Health–Measurement and Treatment Research to Improve Cognition in Schizophrenia New Approaches Conference on social cognition in schizophrenia. During this discussion, the reasons for the recent growth of research on social cognition in schizophrenia were examined. The discussion group established consensus on several points, including the importance of viewing social cognition from interdisciplinary perspectives (including outcomes research, social psychology, cognitive psychology, cognitive neuroscience, and animal models) and the need for clearer definition of terms. There was also general agreement that social cognition is a valuable construct for understanding the nature and disability of schizophrenia. One of the objectives of this group was to generate recommendations for subsequent human and animal studies, and these research agendas are summarized in this report.

Key words: social cognition/schizophrenia/MATRICES/animal models

Introduction

Social cognition refers to the mental operations underlying social interactions, which include processes involved in perceiving, interpreting, and generating responses to the intentions, dispositions, and behaviors of others.^{1–3}

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Phrased another way, social cognition is “the struggle to understand the interdependence between cognition and social behavior,”⁴ or simply put, it is people thinking about people. Social cognitive processes are how we draw inferences about other people’s beliefs and intentions and how we weigh social situational factors in making these inferences. One of the breakout groups at the National Institute of Mental Health (NIMH)–Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) New Approaches Conference (September 2004) focused on the study of social cognition in schizophrenia (cochaired by M. F. Green and B. Olivier). This report presents a brief background on social cognition in schizophrenia and a summary of the recommendations for future research that came from this discussion. We served as the planning committee for the discussion session.

Deficits in social cognition have been well documented using a wide variety of tasks.^{5–7} There have been 2 distinct goals of social cognitive research in schizophrenia: One line of research is devoted to understanding the nature of specific clinical symptoms (e.g., how aspects of social cognition relate to paranoia or thought control); another line of research has been devoted to social cognition’s role in outcome. Indeed, social cognitive deficits appear to be key determinants of functional outcome including social and vocational outcome in schizophrenia.^{8–11} It has been suggested that social cognitive abilities enable subjects to interact effectively with their social environment, and that a lack of certain aspects of social cognition will lead to social misperceptions, unexpected reactions to and from the person, and eventually, social withdrawal.^{5, 12} Hence, for both theoretical and empirical reasons, social cognition appears to be critical to community functioning. In addition to these clinical and outcome goals, there is increasing interest in identifying the neural substrates that underlie social cognitive deficits in schizophrenia. For all of these reasons, further research in this domain is viewed as highly valuable.

The terms, definitions, and subdomains of social cognition used in schizophrenia research vary widely, a fact that impedes communication in the field and makes direct comparison of findings more difficult. Most of the social

cognitive research in schizophrenia has focused in the following areas: emotion processing, theory of mind, social perception, social knowledge, and attributional bias.¹³ As will become apparent, the distinctions among these areas are not always clear-cut. We will briefly define each area.

Emotional processing refers broadly to aspects of perceiving and using emotion, and it relies on separate prerequisite abilities that are in the process of being identified.¹⁴ Recent developments provide the basis for measuring individual differences in these abilities. One influential model of emotional processing, developed by Salovey and colleagues, defines emotional intelligence as a set of skills that combines emotions and cognition. The model includes 4 components of emotional processing: identifying emotions, facilitating emotions, understanding emotions, and managing emotions.^{15–16} *Identifying emotions* involves identifying emotion expressed in faces and pictures. *Facilitating emotions* contains subtests that measure how well participants can evaluate the usefulness of different emotions that best assist a specific cognitive task and behavior. *Understanding emotions* assesses the participant's understanding of blends and changes between and among emotions. Finally, *managing emotions* examines the regulation of emotions in oneself and in one's relationships with others and is similar to the concept of emotional regulation.^{17–18} The boundaries among the various types of social cognition are not absolute, which is another reason for confusion in the terminology in this field. For example, identifying emotions is 1 component of emotional processing but is also sometimes considered to be a component of theory of mind.

Theory of mind is also sometimes referred to as social intelligence, and it typically involves the ability to infer the intentions and beliefs of others.^{19–20} Much of the human literature in this area involves studies of children and has focused on normal versus abnormal development for theory of mind processes. For this reason, many theory of mind measures (e.g., short stories with cartoonlike drawings) were developed for use with children. Measures of theory of mind have been extended to schizophrenia, in part because of the similarity between aspects of social dysfunction in autism and some types of schizophrenia.^{20–21} In schizophrenia the measures of theory of mind have often been modified versions of those used for children, which can sometimes create problems in obtaining an adequate range in performance for adult schizophrenia patients. Some newer measures have been specifically developed for adults; an example is a test that captures theory of mind processes in daily conversations, such as forming inferences about others' intentions and beliefs.²²

Studies of *social perception* typically assess the ability to judge social roles and rules (intimacy and status) and social context.^{23–25} Social perception has similarities to emotion perception but differs in the type of judgment

required. In contrast to emotion perception tasks that require participants to evaluate emotional qualities in facial expressions or voice tone to infer someone's mood, social perception tasks require participants to use social cues to infer the situational events that generated the social cue. These tests may ask subjects to identify interpersonal features in the situation such as intimacy, status, mood state, and veracity. Hence, social perception can also refer to one's perception of relationships between people, in addition to perception of cues that are generated by a single person.²⁶

Social knowledge (also called social schema) refers to the awareness of the roles, rules, and goals that characterize social situations and guide social interactions.^{27–28} Examples include a subject's knowledge of the role of a doctor in a clinic or the goals of a customer who is talking to a waiter in a restaurant. This area interfaces closely with social perception because the identification of social cues frequently requires some knowledge of what is typical in specific social situations.

Attributions refer to how one explains the causes for positive and negative outcomes and how the meaning of events is based on one's attribution of their cause. Attributions can be measured via questionnaires such as the Internal, Personal, and Situational Attributions Questionnaire (IPSAQ).²⁹ The IPSAQ allows for a distinction between external "personal" attributions (i.e., causes that are attributed to other people) and external "situational" attributions (i.e., causes that are attributed to situational factors) and "internal" attributions (i.e., causes that are due to oneself). This distinction is in accord with the clinical experience of individuals with persecutory delusions, who often explain negative outcomes (e.g., someone not returning a phone call right away) as being due to malevolent intentions (e.g., that person is angry at him or her) rather than to a situational context (e.g., the person is out of town). In general, individuals with persecutory delusions show a tendency to attribute negative outcomes to others, rather than situations, or what has been called a "personalizing bias."^{30–31}

Social cognition in schizophrenia is a central topic for the NIMH-MATRICES initiative because it is 1 of the 7 domains represented in the MATRICES Consensus Cognitive Battery for clinical trials in schizophrenia.³² The domains for the cognitive battery were initially selected through careful examination of factor-analytic studies of cognition in schizophrenia,³³ and they include speed of processing, attention/vigilance, working memory, verbal learning, visual learning, and reasoning and problem solving. When these initial 6 factors were presented at the first MATRICES consensus meeting in April 2003, there was clearly expressed concern from the participants about the omission of social cognition. The MATRICES Neurocognition Committee had not proposed social cognition as 1 of the domains because there were few standard social cognition measures used in schizophrenia and it was not

represented in factor-analytic studies. Also, it was believed that measures of social cognition in schizophrenia had not yet achieved a level of standardization comparable to that of other cognitive measures. Nevertheless, it was pointed out at the consensus conference that published and unpublished studies from several laboratories have shown that social cognition is closely related to functional outcome in schizophrenia and may be a mediating variable between basic (nonsocial) cognition and functional outcome.³⁴ Additional arguments for including social cognition came from cognitive neuroscience and the suggestion that certain measures of social cognition may have a distinctive neural substrate from some of the systems that support the nonsocial cognitive domains.^{35–41} These studies indicate that certain social cognitive tasks activate particular neural circuits; however, the interesting question of whether there are neural substrates dedicated to social processing remains unanswered.^{42–43}

From presentations and feedback at the consensus conference, as well as subsequent discussion, the MATRICS Neurocognition Committee voted to add social cognition as a domain to be represented in the battery. Based on consideration of essential test criteria (i.e., test-retest reliability, utility as a repeated measure, relationship to outcome, and practicality/tolerability), the Managing Emotions component of the Mayer-Salovey-Caruso Emotional Intelligence Test was selected for inclusion in the MATRICS Consensus Cognitive Battery.

In addition, for social cognition to be useful for drug discovery, preclinical scientists will need animal models for the relevant cognitive domains that can be used to screen novel compounds for potential efficacy. There was considerable discussion in the breakout group about the availability of animal models for social cognition. Rodent behavioral tasks include measures of social approach and withdrawal, social interaction, social communication, social recognition, social memory, social preference, and social motivation. Rats and mice are social species that often live in colonies and sleep in group nests. Home cage observations provide simple measures of normal sociability. Failures to build nests, sleep together in the nest, or rest in group huddles may provide early indicators of aberrant social behavior, as demonstrated in mice with a null mutation in a developmental gene, *disheveled-1*.⁴⁴ Social approach by a subject mouse has been measured in test equipment where an unfamiliar stimulus mouse is enclosed in a tube, contained in an open wire cage, or tethered within the chamber.^{45–48} Social interaction is scored as sniffing, following, climbing on, allogrooming, juvenile play, fighting, and sexual interactions.^{49–50} Social interaction deficits were demonstrated in a rat neonatal hippocampal lesion model of schizophrenia.⁵¹ Social communication may include ultrasonic vocalizations emitted by pups separated from mother and nest and parental retrieval responses to the pup vocalizations⁵² and vocalizations emitted by juveniles and

adults engaged in social interactions,⁵³ although the communication intent of these ultrasonic vocalizations in rodents is unclear. Deposition of urinary olfactory scent markings and responses to social odors such as soiled cage bedding were useful markers in the discovery of a social deficit in vasopressin receptor 1b mutant mice.⁵⁴

Social recognition and social preference are measured in choice tasks, wherein the subject rat or mouse is given access to 2 conspecifics, 1 familiar and 1 unfamiliar, and the time spent with each is quantitated.⁵⁵ Social memory tasks incorporate a time delay of several hours or days between presentations of the 2-choice stimulus mice. Insel and coworkers at Emory University have demonstrated selective deficits in social memory in oxytocin-null mutant mice using a 2-choice social task.⁵⁶ Social motivation has been tested in an operant chamber, in which the rat must press a lever to gain access to a social partner.⁵⁷

Discussion focused on the extent to which these rodent models assess social behavior versus social cognition, *per se*. The evidence for selective deficits in social memory in oxytocin-null mutant mice seems very analogous to that for human social cognition, whereas the connections for other rodent models are less obvious. It is likely that certain social cognitive constructs (e.g., theory of mind) will require animal models of other species, such as nonhuman primates. The animal models may provide insights into the basic building blocks of social cognition, if we can understand better their cognitive components. Considerable thought and effort will need to be invested to optimize and apply components of these social tasks to directly address social cognition hypotheses in rodent models of schizophrenia.

Recommendations

One of the key goals of the breakout group was to generate a research plan for subsequent research into social cognition in schizophrenia. The group broke this task into 3 components: a short-term research agenda for human studies, a longer-term agenda for human studies, and an agenda for animal models. Each of these will be considered separately.

Human Studies: Short Term (Next 3–5 Years)

The short-term agenda focuses on agreement on the definition, measures, and factors of social cognition:

- conduct “mini-MATRICES” process to agree on areas that should be included in the study of social cognition in schizophrenia: for example, social cue perception, affect perception, theory of mind, attributional style, and so on
- increase input from experimental social psychology
- refine measures (e.g., scaling challenges in moving from children to adults)

- collect data on drug effects on social cognition (e.g., antipsychotic medications, novel compounds)
- collect data from larger neurocognitive batteries to examine factor structure (both within social cognition and between social and nonsocial cognition)

For the short-term research goals, the focus is on tasks that will help to organize the field and enhance communication among researchers. Several obstacles to the integration of research findings include the lack of agreement on terms and definition, as well as the absence of consensus on how to divide the field of social cognition into subdomains. In many respects, these definitional challenges are similar to those encountered by MATRICS in the area of cognitive deficits in schizophrenia. In contrast to the situation for cognitive performance assessment, there was no strong suggestion that social cognition needs a standard assessment battery at this point in time. It was thought that a high degree of standardization would not be desirable for a field that is relatively early in development.

Several questions emerged related to the nature or factor structure of social cognition. One question is whether the social cognitive assessments that are used in schizophrenia reflect a single factor, or if they are better viewed as a cluster of separate factors (e.g., social perception tests versus theory of mind tests). A second question is whether the social cognition tests tend to form a separate factor (or factors) from basic (nonsocial) cognition tests. A third question is whether the inclusion of social cognition provides added value above and beyond that provided by basic cognition. Support for added value comes from a recent study with structural equation modeling showing that a measure of social perception had a unique relationship to community outcome after controlling for visual perceptual processes.³⁴

A recurring theme in the discussions was the need for clinical researchers to obtain input from basic behavioral scientists who do not work directly with clinical populations but who have a broader understanding of the social cognitive area. This theme is congruent with the current NIMH emphasis on enhancing translational research from basic behavioral science to clinical research. One of the short-term goals is to increase communication between clinical investigators and social psychologists who are experts in social cognition; such interactions could lead to adapting innovative assessment methods for use in clinical samples.

Human Studies: Longer Term (Next 5–10 Years)

The longer-term goals for human studies are less specific than the short-term goals, and they focus on increasing the interface between social cognition to cognitive neuroscience:

- support studies of neuroimaging, electrophysiology, brain damage, and pharmacology to identify neural substrates of social cognition performance in schizophrenia
- use neuroscience information to develop behavioral methods that parse social cognition into subcomponent processes
- assess the similarities and differences of identified neural substrates to basic (nonsocial) cognition

Recent work in affective neuroscience has been successful in identifying the neural substrates of social cognitive processes, and the clinical extension of this research would be to identify the substrates of performance differences between patients and controls. One key question in this area is the degree of overlap in the neural circuits that underlie social versus basic cognitive performance tasks. In terms of schizophrenia, it would be valuable to know the degree of overlap between the circuits that underlie deficits in basic cognition versus those that underlie deficits in social cognition. There is also the question of whether specific types of social cognition arise through computational processes that are similar to those in basic cognition, even though different brain regions may be involved. For example, it has been proposed that theory of mind involves a higher-level manifestation of the same neural synchronization and binding processes that characterize the integration of information into coherent representations in other neurocognitive domains,⁵⁸ as is suggested by relationships among impaired theory of mind, reduced perceptual organization, and conceptual disorganization.^{59–60} Although much of the discussion about cognitive neuroscience involved the potential value of functional neuroimaging, the participants clearly indicated that other methods, including electrophysiology and psychopharmacology, would yield complementary information.

Translation of Social Cognition Into Animal Models

The final research agenda involves the development of animal models for social cognition. This component focuses on the following:

- develop new tasks for rodents with conceptual links to social cognition
- develop tasks that can measure both social cognition and social motivation
- explore (with lesion, pharmacology, genetic approaches) the neural substrates of social learning in animals
- explore the overlap between social cognition and negative symptoms in animals and humans

Considering the goals of the MATRICS initiative, the development of animal models is an essential part of the

preclinical testing of promising cognition-enhancing compounds. Whereas some aspects of social cognition do not have obvious animal analogues at the level of rodents (e.g., theory of mind), others clearly do (e.g., social perception, emotion processing). As mentioned above, social cognitive constructs that are not appropriate for rodents may be appropriate for nonhuman primates.

The members of the breakout group were impressed with the creativity and diversity of the animal models for social cognition that currently exist while acknowledging that validation of many of these models (e.g., comparable effects of psychopharmacology in both animal and human tasks) is still incomplete. One interesting feature of the animal models is that they can separate social motivation from social cognition. This distinction is potentially important, but the discussion spent little time on the topic of human assessment of social motivation, partly because this construct is sometimes viewed as a negative symptom. Nonetheless, the group believes that the field will benefit from a clearer understanding of whether it is desirable, or even possible, to separate social motivation from social cognition for separate investigation. One particularly difficult challenge is how to separate animal models of social motivation and social cognition from those of negative symptoms.

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