Implications for the Neural Basis of Social Cognition for the Study of Schizophrenia

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Objective: The study of social cognition in schizophrenia has received growing attention in recent years. At the same time, a large body of work has explored the neural basis of social cognition in both nonclinical and clinical groups, other than those with schizophrenia. The gap between these two literatures is considerable and may slow progress in creating a comprehensive social cognitive model of schizophrenia. This article attempts to bridge this gap by discussing how the neural basis of social cognition may inform future clinical research in schizophrenia.

Method: PsycINFO and MEDLINE were systematically searched for articles pertaining to the neural basis of social cognition and social cognition in schizophrenia. Relevant studies were obtained and synthesized into a comprehensive review and integrative formulation.

Results: Striking parallels between these two areas of research were found.

Conclusions: These parallels might help to better elucidate the underlying mechanisms for social cognitive and social behavioral impairments in schizophrenia as well as provide potential targets for treatment and drug development.

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Impairments in social functioning are among the hallmark characteristics of schizophrenia (DSM-IV), and these impairments, although present in other clinical disorders (e.g., bipolar disorder), are most pronounced in persons with schizophrenia (1). Deficits in social functioning are present throughout the course of the disorder. For instance, they are frequently present in patients having a first episode, may persist despite antipsychotic treatment, and tend to remain stable in severity or even worsen in subsequent phases of the illness (2). Deficits in social functioning are also present before the onset of psychosis (3) and are evident in individuals with a biological parent who has schizophrenia (4), suggesting that these deficits are premorbid features of—and may be a vulnerability factor for—schizophrenia. In addition to being implicated in the development of schizophrenia, impairments of social functioning contribute to the rate of relapse (5). Therefore, it appears that impairments in social functioning represent a core behavioral feature of schizophrenia. These findings not only underscore the importance of social dysfunction in the course of schizophrenia but also suggest that any interventions, psychosocial or pharmacological, that can affect social functioning may have crucial implications for long-term outcome.

In an effort to better understand the processes underlying social dysfunction in schizophrenia, great attention has been given to the role of neurocognitive skills (e.g., attention) in supporting social behavior. The logic of this approach is that adequate neurocognitive skills either support functionality or facilitate the acquisition of interpersonal skills (6). And, in fact, reviews of the literature support the association, both cross-sectional and longitudinal, between neurocognition and psychosocial dysfunction in schizophrenia (7–10). Despite these findings, it is important to remember that the relationship between neurocognition and psychosocial functioning is modest (9, 10). Because of these modest associations, investigators have more recently sought to examine specific and unique aspects of cognition that underlie social function that may be functionally distinct from traditional neurocognitive domains. The term "social cognition" thus indicates other aspects of cognition that are not typically assessed by traditional neurocognitive tasks but that potentially have an independent link to social behavior and social function.

In this article, we present an overview of social cognition in schizophrenia. Unlike an earlier article that focused predominantly on the psychological aspects of social cognition in schizophrenia (9), this article will emphasize the neural basis of social cognition and its potential relevance to the understanding of psychosocial dysfunction in schizophrenia. We begin by reviewing the concept of social cognition and what distinguishes it from traditional neurocognition (or nonsocial cognition). We will then discuss the relevance of social cognition in schizophrenia, with an emphasis on the functional significance of social cognitive biases and deficits. This will be followed by a review of the neural structures that have been implicated in social cognition in both nonclinical and clinical groups, with an eye toward applying these findings to the neurobiology of schizophrenia. This article will conclude with suggestions for future research in this area.

Definition of Social Cognition

Definitions of social cognition range from the basic (e.g., "Social cognition is simply thinking about people,") (11) to the more complex (e.g., "the ability to construct representations of the relations between oneself and others, and to use those representations flexibly to guide social behavior") (12). For the purposes of this review, social cognition will refer to "the mental operations underlying social interactions, which include the human ability to perceive the intentions and dispositions of others" (13) and "the processes that subserve behavior in response to conspecifics (other individuals of the same species), and, in particular, to those higher cognitive processes subserving the extremely diverse and flexible social behaviors that are seen in primates" (14). These definitions firmly link social cognition to social behavior and include such processes as "theory-of-mind" skills, social perception, and attributional style.

There is evidence from clinical groups for the relative independence of social cognition from other aspects of cognition. For example, individuals with either frontal or prefrontal cortex damage show impaired social behavior and functioning, despite the retention of intact cognitive skills such as memory and language (15–17). The fact that social cognition can become selectively impaired after such an injury while sparing nonsocial cognition suggests that unique neural circuits subserve social cognition. A similar dissociation between social cognition and nonsocial cognitive skills is often observed in persons with prosopagnosia, who show selective impairments in the perceptions of faces but preserved perception for nonsocial stimuli (18). Such findings have led Kanwisher (18) to conclude that facial processing is a result of domain-specific, rather than general, neural mechanisms.

Even more compelling evidence for the autonomy of social cognition is gleaned from studies of persons with Williams's syndrome and persons with autism. Individuals with Williams's syndrome tend to be outgoing and social, despite having below-normal intelligence (19). These individuals appear to have relatively preserved basic social cognitive skills (i.e., facial processing and simple abilities regarding the theory of mind [20, 21]), despite having deficits in spatial cognition (22, 23). This partial preservation of social cognition is in direct contrast to persons with high-functioning autism and Asperger's syndrome, who show specific impairments in social cognition and social behavior that are not related to general cognitive abilities (24, 25). These findings lend support for the hypothesis that specific neural modules exist that are devoted to the processing of social information, a hypothesis that has also been maintained in the areas of evolutionary biology and primatology (9, 12, 26, 27).

Why Study Social Cognition in Schizophrenia?

Deficits and Biases in Social Cognitive Performance

The study of social cognition in schizophrenia has generally focused on theory-of-mind skills, social perception, and attributional style. Theory-of-mind skills refers to the ability to represent the mental states of others and/or to make inferences about another's intentions. Relative to nonclinical comparison and clinical control participants, individuals with schizophrenia perform poorly on tasks that measure theory-of-mind abilities (28–34) (see reference 35 for a review), although the evidence is mixed regarding whether impairments in theory-of-mind skills are independent of a general cognitive deficit (36) (however, see references 29, 31, and 37). Additionally, impairments of theory-of-mind skills are most profound among individuals with negative features, passivity symptoms, behavioral signs, and paranoid symptoms (28, 30, 38). This suggests that theory-of-mind skills are sensitive to the heterogeneity of schizophrenia. Finally, evidence also suggests that impairments of theory-of-mind skills are most pronounced during acute psychotic episodes and that performance on theory-of-mind tasks may improve during remission (29, 30).

Studies of social perception in schizophrenia can be broken down into two general areas: facial affect recognition and social cue perception. Reviews of the literature on facial affect recognition (i.e., references 9 and 39–42) suggest the following. First, individuals with schizophrenia have deficits in facial affect perception compared to nonclinical comparison participants. Second, these deficits are present relative to other psychiatric disorders, such as depressive disorder; however, results are inconsistent when compared to disorders that include psychotic features, such as bipolar disorder. Third, greater impairment is evident for the perception of negative emotional displays compared to positive displays, with perhaps the greatest impairment for the perception of fear (43, 44). Fourth, longitudinal studies support a stable deficit in emotion perception (45, 46), although there is some evidence that individuals whose symptoms are in remission may perform better on tasks that measure affect perception than individuals who are in an acute phase of the disorder (47, 48). Fifth, there is some evidence that individuals with paranoid schizophrenia are better at facial affect perception than individuals with nonparanoid subtypes of the disorder (49–51) (see reference 52 for an exception). And, finally, the jury is still out regarding whether deficits in facial affect perception are part of a generalized performance deficit (53–56) or whether they are specific to decoding only facial emotions (e.g., references 57 and 58).

Unlike recognition stimuli for facial affect, tasks that assess perception of social cues use more dynamic stimuli that require multiple sensory modalities. Persons with

schizophrenia show consistent impairments in social cue perception (59–62); these impairments are most pronounced for abstract relative to concrete social cues (63). Specifically, when presented with videotapes of persons interacting, individuals with schizophrenia have more difficulty discerning the goals and intentions of target people than what they are wearing or saying—a finding consistent with what we expect from individuals who have difficulties in discerning the intentions of others (i.e., theory-of-mind skills).

Most of the work on attributions in schizophrenia has focused on investigating the role of attributional style in hallucinations and delusions (i.e., how one explains positive and negative outcomes). Bentall (64) has argued that individuals who experience hallucinations are biased toward making external attributions for their perceptions, that is, that they attribute internal perceptual events to an external source (65). Individuals with persecutory delusions tend to show an exaggerated self-serving bias (i.e., attributing negative outcomes to others and positive outcomes to one's own actions) (see references 66 and 67 for reviews; for partial failures to replicate this finding, see references 68 and 69), although this effect may be stronger for attributing negative outcomes to others rather than for taking credit for success (70). Finally, it appears that for negative interpersonal events, persons with paranoia and/or persecutory delusions are more likely to blame others rather than the situation or circumstances than persons without paranoia and/or persecutory delusions (66, 71).

Functional Significance of Social Cognition in Schizophrenia

There is growing evidence that social cognition is related to social impairments in schizophrenia, even after control for performance on neurocognitive tasks (72). In a series of studies, facial affect perception was shown to have a moderate association with social functioning among both inpatients (55, 73) and outpatients with schizophrenia (74). Furthermore, Ihnen et al. (74) found that the best predictor of social skill was the participants' perceptions of their own social performance or self-perception. This finding was strengthened in a reanalysis of the Ihnen et al. data, which found that persons with schizophrenia who had high self-monitoring skills (i.e., awareness of the impact of their behavior on other people) had better social skills than persons with schizophrenia who had low self-monitoring skills (75). This difference in social skills could not be accounted for by group differences in verbal IQ or education.

There is also evidence that social knowledge and general social perception are related to social functioning among persons with schizophrenia. Specifically, the ability to identify the sequence of behavioral steps used in social situations and to place them in the correct order is related to behavior in the treatment setting among chronically ill inpatients (73, 76) and persons recovering from an acute psychotic episode (77). Furthermore, social cue perception has shown a relationship with in vivo social skills (78–80), although in the study by Bellack et al. (78), this relationship held only in situations involving negative affect. Finally, Hooker et al. (81) found that, relative to a nonclinical comparison group, individuals with schizophrenia showed impairments in counterfactual thinking (i.e., the ability to think about the alternative ways in which one would have handled a problem situation); this performance difference could not be accounted for by group differences in IQ. Furthermore, better counterfactual thinking was associated with higher functioning (based on the score on the Global Assessment of Functioning scale) among the patients with schizophrenia.

The foregoing provides strong evidence for the functional significance of social cognition in schizophrenia. Perhaps most impressive is that in a few studies (73, 75, 79, 81), the association between social cognition and social functioning could not be accounted for by cognitive deficits. These findings lend support to the hypothesis that social cognition contributes independent variance to functional outcomes beyond nonsocial cognition alone.

The Neurobiology of Social Cognition

In 1990, Brothers (13) proposed a neural system of social cognition that was composed of the orbitofrontal cortex, the superior temporal sulcus, and the amygdala. This seminal article led to numerous studies that have generally confirmed the role of these neural structures in social information processing (12, 82–85) as well as several others that may play secondary roles (i.e., the right parietal cortex, the insular cortex, the basal ganglia [82], the temporal-parietal junction at the top of the superior temporal gyrus, and the temporal poles [86]). Although these neural structures also subserve other cognitive functions (e.g., problem solving and conceptual reasoning), they and not other neural structures tend to be most consistently activated in response to social stimuli, thus underscoring their role in neural models of social cognition. In what follows, we describe the major neural structures and mechanisms that have consistently shown a role in social cognition, particularly those found to be impaired in schizophrenia. An in-depth treatment of each brain region would far exceed the scope of this article; thus, we limit our discussion to the specific areas proposed by Brothers (13) and others (12, 14, 82) as subserving social cognition: the medial prefrontal cortex, the superior temporal sulcus, the fusiform gyrus, the amygdala, and the ventromedial prefrontal cortex. We begin with a discussion of the medial prefrontal cortex and its role in theory-of-mind skills.

The Frontal Cortices and the Theory of Mind

There is growing evidence that performance on theory-of-mind tasks is associated with activation of specific frontal cortical regions, in particular, the medial frontal cortex and the medial prefrontal cortex. A limited number

of studies also support the role of the orbitofrontal cortex in theory-of-mind tasks. Early studies that attempted to localize theory-of-mind skills in the brain examined regions that were activated in healthy participants during a theory-of-mind task. Fletcher et al. (87) used positron emission tomography (PET) to examine neural activation while healthy participants read passages and answered questions about each passage. The passages were either a story that required the attribution of mental states (a theory-of-mind story), a story that did not require the attribution of mental states (a non-theory-of-mind story), or a series of unlinked sentences. Comparisons of brain activity during each type of passage revealed a unique activation of Brodmann's areas 8 and 9 in the left medial frontal cortex for the theory-of-mind stories. Similarly, Goel et al. (88) found selective activation of the left medial frontal cortex (Brodmann's area 9) throughout a theory-of-mind task in which normal participants were asked to infer the thoughts of a contemporary of Christopher Columbus. Thus, results from these early studies indicated that theory-of-mind skills were specific to the medial frontal cortex (see also reference 89 for more recent support of the role of the medial frontal cortex in theory-of-mind tasks).

More recent studies have used both verbal and nonverbal tasks in their experimental designs and have supported the role of the prefrontal cortex (90, 91), specifically the medial prefrontal cortex, including portions of Brodmann's areas 8 and 9, in theory-of-mind skills. Gallagher and colleagues (92) used functional magnetic resonance imaging (fMRI) to assess brain activity while participants read and answered theory-of-mind questions about a verbal passage and interpreted and explained the meaning of cartoons that required theory-of-mind skills. Relative to control conditions, there was unique activation of the medial prefrontal cortex during the theory-of-mind tasks. Similar results were found when using only a cartoon task (93); the cartoons that required the attribution of intentions to others invoked a selective activation of the medial prefrontal cortex while the cartoons that reflected only physical logic did not. Additionally, the medial prefrontal cortex has also been implicated in theory-of-mind tasks that use nonhuman stimuli. Castelli and colleagues (94) found that the medial prefrontal cortex was selectively activated when the movement patterns of geometric shapes evoked mental state attribution but not during simple action description.

As mentioned earlier, individuals with autism and Asperger's syndrome display significant deficits in theory-of-mind skills. Therefore, a second approach to identify the neural structures involved in theory-of-mind skills has been to compare the patterns of brain activation in healthy individuals to that of individuals with autism or Asperger's syndrome. Happe et al. (95) compared PET scans taken during a theory-of-mind task of five individuals with Asperger's syndrome to those of normal volunteers; the patterns of activation were identical except for a portion of Brodmann's areas 8 and 9 in the medial prefrontal cortex, which was activated in the healthy participants but not in the individuals with Asperger's syndrome.

Additional studies have also implicated the orbitofrontal cortex in theory-of-mind skills. Baron-Cohen et al. (83) used single photon emission computerized tomography to identify areas of activation during performance on a mental-state terms task (a theory-of-mind task). They found greater cerebral blood flow (CBF) in the right orbitofrontal cortex of healthy participants during a theory-of-mind task but not during a control task. Lesion studies also lend support to this pattern of findings. Stone et al. (84) found that individuals with bilateral orbitofrontal lesions performed similarly to individuals with Asperger's syndrome on a task requiring the recognition of a faux pas, a task that requires social reasoning as well as theory-of-mind skills.

The foregoing suggests that activation of the medial prefrontal cortex and, to some extent, the orbitofrontal cortex is critical to being able to infer the mental states of others (see reference 86 for two additional brain regions that are activated during theory-of-mind tasks but that are not within the scope of this article). This finding is consistent with the structural and activation deficits found in schizophrenia. Persons with schizophrenia appear to have a smaller brain volume and larger ventricles than individuals without schizophrenia (96). A meta-analysis of 58 studies (97) concluded that the mean cerebral volume of individuals with schizophrenia was 98%, assuming 100% in nonclinical comparison subjects, and that the mean ventricular volume was 126%. More specifically, neuroimaging studies have consistently found alterations in the frontal cortex, including the medial and orbitofrontal cortex, in individuals with schizophrenia (98, 99). This smaller brain volume is shown in both smaller gray and white matter volumes in the frontal and temporal lobes (100–102) and remains, even when compared to healthy siblings (103). However, there is some evidence that the severity of negative symptoms is found to be associated with specifically smaller prefrontal white matter volumes (104).

Consistent with overall smaller cerebral volumes, the prefrontal cortex of individuals with schizophrenia is characterized by smaller neuronal size (105); men with early-onset schizophrenia display smaller gray matter volumes in the medial frontal gyrus, Brodmann's area 9 (102). Along with smaller volumes, functional imaging has revealed decreased regional (r)CBF in the left medial frontal gyrus (Brodmann's area 9) during a cognitively nondemanding visual fixation task (106), in the left medial prefrontal cortex during the Wisconsin Card Sorting Test, and in both the left and right medial prefrontal cortex during test and rest conditions among persons with schizophrenia (107). Finally, persons with schizophrenia show evidence of hypoactivity of the right medial prefrontal cortex during cognitive tasks such as time estimation and frequency discrimination (108).

Overall, the evidence for decreased rCBF during cognitive tasks is compelling, and research has extended this finding to social cognitive tasks. Specifically, Russell et al. (109) found that in relation to comparison participants, individuals with schizophrenia made more errors in mental state attribution and showed less activation of the middle frontal cortex, which includes part of Brodmann's area 9, during a theory-of-mind task. This finding is particularly important since it provides a link between activation deficits in schizophrenia and impaired performance on a theory-of-mind task.

Facial and Emotion Processing

Several reviews have established that specific regions of the brain are associated with facial and emotional perception. Among these are the lateral fusiform gyrus, the superior temporal sulcus, and the amygdala (12, 82, 85). The lateral fusiform gyrus subserves selective activation to faces (110, 111), and because of this area's specificity and the consistency with which it has been linked to facial recognition, it has been dubbed the "fusiform face area." In some ways, facial perception is a basic building block of social cognition since it is a likely first step in the social communication process. And, in fact, Brothers (13) referred to facial recognition as a "lower-level subprocess of social cognition."

Once a given social target is identified, the next step in the social communication process is to determine if that target is willing to interact, is approachable, etc. This type of social information is gleaned from changeable aspects of the face, such as the eyes and mouth. Changes in the direction of gaze indicate the focus of one's attention, and changes in the shape of the eyes and mouth facilitate emotional expression and indicate emotions such as happiness and aggression. This distinction between simple identification and complex emotional recognition suggests that the processing of static and dynamic facial features may have physically distinct loci in the brain. Indeed, findings indicate that this is the case since the superior temporal sulcus is more strongly activated during tasks focusing on visual gaze, while the lateral fusiform gyrus tends to be more strongly activated during tasks focusing on identity (112). Thus, it appears that the region of the superior temporal sulcus is involved in processing the changeable aspects of the face, while the lateral fusiform gyrus processes nonchangeable aspects of the face (112).

The third neural structure implicated in facial and emotional processing is the amygdala. Both lesion and imaging studies have consistently supported the role of the amygdala in recognizing faces and emotions (113). Specifically, individuals with damage to the amygdala are noted to have difficulty recognizing faces and judging the emotional expressions of others, particularly when that expression is fear (114–116). The amygdala has also been implicated in threat detection. Adolphs et al. (117) asked three individuals with complete bilateral amygdalar damage and seven individuals with unilateral amygdalar damage to rate faces for approachability and trustworthiness. All three bilateral participants judged the faces to be more approachable and trustworthy than comparison participants, and this was most notable for faces that the comparison participants rated the least approachable and trustworthy. This finding, in conjunction with the fact that persons with amygdalar damage have the most difficulty recognizing fear, suggests that the amygdala may be more closely linked to the recognition of negative emotions than those of a positive nature. Imaging studies in healthy volunteers support this conclusion. Using PET, Morris et al. (118) found a differential response in the amygdala to fear and happiness. Amygdalar activation was much more pronounced when participants viewed photographs of fearful faces, and there appeared to be an interaction between the level of activation and the intensity of emotion such that the more fearful a face looked, the greater the level of activation. Whalen et al. (119) also explored the differential amygdalar response to fear and happiness. Photographs of happy and fearful expressions were presented in a backward-masking procedure that resulted in a majority of the participants being unaware of seeing fearful and happy expressions, and despite a lack of conscious awareness, significantly greater amygdalar activation was noted in response to fearful faces. A similar study that did not use backward masking used fMRI to compare amygdalar activation in response to fear and disgust. The results indicated that the amygdala was only activated when viewing fearful faces and not when viewing disgusted or neutral faces (120). Overall, findings from lesion and imaging studies clearly indicate that the amygdala is important for emotional recognition and suggest that the amygdala may play a disproportionate role in the processing of negative or threatening stimuli (121).

Although, to our knowledge, no studies have examined abnormalities in the superior temporal sulcus in individuals with schizophrenia, there is convincing evidence for the potential role of the fusiform gyrus and amygdala in schizophrenia. Like the medial prefrontal cortex, the fusiform gyrus shows abnormal volume and blood flow in persons with schizophrenia. Both McDonald et al. (122) and Paillere-Martinot et al. (102) found smaller regional gray matter in the left fusiform gyrus of individuals with schizophrenia in relation to healthy comparison subjects, and Malaspina and colleagues (106) reported increased rCBF in the right fusiform gyrus during a visual fixation task. Although the latter finding may initially seem counterintuitive, one must consider that increased rCBF was not present in healthy comparison participants and, in this respect, may indicate an abnormality in individuals with schizophrenia. It should be noted, however, that it is unknown whether the noted increase in rCBF would occur during a comparable social cognitive task.

The amygdala in individuals with schizophrenia appears to be smaller than in individuals without schizophrenia.

Although initial reports could not agree on a smaller unilateral or bilateral volume (see, e.g., references 123 and 124), more recent studies have confirmed a smaller bilateral volume (125). The meta-analysis by Wright et al. (97) supports this conclusion by reporting that the average volume of the amygdala in an individual with schizophrenia is only 94% of that in a healthy individual. There is also evidence that amygdalar activation is abnormal in individuals with schizophrenia, particularly when negative affect is involved. Schneider and colleagues (126) used mood induction in both persons with schizophrenia and normal comparison subjects and showed that persons with schizophrenia had reduced amygdalar activation during sadness, despite self-ratings of sadness that were comparable to that of comparison subjects. In addition, a functional imaging study of individuals with schizophrenia during an emotion recognition task showed that relative to healthy comparison participants, individuals with schizophrenia were not only less accurate in identifying emotions, but they also displayed no amygdalar activation to fearful expressions (127). Thus, it appears that the neural structures involved with facial and emotional perception are not only smaller in individuals with schizophrenia but also show abnormal patterns of activation that are associated with performance on emotional recognition tasks.

The Ventromedial Prefrontal Cortex, Social Knowledge, and Behavior

Work linking the ventromedial prefrontal cortex to social knowledge and behavior has primarily involved lesion/brain injury studies in both primates and humans (see references 14 and 113 for reviews). In nonhuman primates, lesions of the frontal cortices have been associated with abnormal social behavior such as isolation and avoidance. In humans, ventromedial prefrontal lesions have been associated with the inability to incorporate emotional knowledge into cognitive processes (e.g., using emotional hunches to discriminate between choices), as well as a lack of normal emotional responses, and difficulty with social reasoning and decision making (128, 129). Adolphs (14) has reported that participants with ventromedial lesions were more accurate than comparison participants when reasoning about nonsocial scenarios but less accurate than comparison subjects when reasoning about social situations. In addition, observations of individuals with prefrontal cortex lesions have revealed an inability to generate appropriate responses to social situations and to reason through social dilemmas, despite normal intellectual functioning (15). Thus, it appears that the ventromedial prefrontal cortex plays a role in social behavior and reasoning.

To our knowledge, no research has directly examined the ventromedial prefrontal cortex in schizophrenia, so it is not possible to draw any firm conclusions at this time. However, we do know that individuals with schizophrenia are less skillful than nonpatient comparison subjects in understanding the sequence of actions that comprise social situations (80, 130) and score significantly lower on tasks that measure knowledge of social situations (131). Thus, given the pattern that has emerged with the other brain areas, we can speculate that individuals with schizophrenia may also demonstrate abnormalities of the ventromedial prefrontal cortex, which may influence their performance on tasks requiring social reasoning or social knowledge.

Conclusions and Future Directions

In this article, we reviewed the neurophysiology underlying social cognition and provided support for the importance of social cognition as an aspect of cognition relatively independent of nonsocial cognition. Furthermore, we presented a growing body of evidence that social cognition has functional significance in schizophrenia, adding variance independent of nonsocial cognition to social performance. Finally, we pointed out that the neurobiology of social cognition, mainly in the areas of the prefrontal cortex and amygdala, is consistent with the neural deficits found in schizophrenia, suggesting a common biological mechanism underlying social cognitive impairments and psychosis.

There is still a great deal of work ahead in the study of social cognition and schizophrenia. Despite the fact that high-risk and follow-back studies indicate that impairments in social functioning predate the onset of schizophrenia (3, 132–140), there has been little work on the role of social cognition in the development of psychosis. The most notable exception is the finding that an external locus of control in adolescence, which is similar to attributional style, was predictive of poor mental health in adulthood in an Israeli high-risk study (141). Additionally, Cornblatt and colleagues (142) have long hypothesized that deficits in social information processing might mediate the relationship between nascent cognitive deficits in childhood and subsequent behavioral difficulties in adolescence and adulthood in persons with schizophrenia. Unfortunately, this provocative hypothesis has gone untested.

As mentioned, there is growing evidence for the functional significance of social cognition in schizophrenia. However, studies that have examined the role of social cognition in the social functioning of persons with schizophrenia have used primarily cross-sectional designs, thus limiting their applicability to understanding the course of the disorder. Furthermore, research in this area has examined only the role of emotion and social perception on social behavior, giving almost no attention to the potential functional significance of the theory of mind and attributional style. Attention has focused exclusively on their role in positive symptoms (see references 35 and 66 for reviews).

Finally, there has been little direct work on examining the neural processes underlying social cognition in schizo-

phrenia. Most of the emphasis in this area has been on understanding the biological mechanisms underlying neurocognition, which is consistent with the interest in the cognitive factors underlying social functioning (8) and treatment (e.g., cognitive remediation) (143).

Future studies on the neurobiology of social cognition may shed light on resolving the heterogeneity of schizophrenia, particularly with respect to the variety of impairments in social functioning found in this disorder. For example, as stated earlier, the amygdala has been implicated in threat detection. This leads to the question of whether amygdalar activation varies as a function of schizophrenia subtype; individuals with persecutory delusions may show overactivation, which results in a long-term bias toward processing (or seeking) threatening information, while those of another subtype (or predominantly negative symptoms) may demonstrate amygdalar underactivation (resulting in the oft-cited emotional perception deficits of schizophrenia). Such activation characteristics may subsequently relate to the actual behavior of persons with schizophrenia; overactivation of the amygdala could be associated with a personalizing attributional style (i.e., blaming others, rather than situations, for negative outcomes) and subsequent paranoid-type behaviors (e.g., acting in a hostile manner toward another person, perceiving someone in a negative manner, desiring greater social distance from another person) (144). It is only when a link between neurobiology, neurocognitive/social cognitive mechanisms, and behavior/symptoms is established that a truly comprehensive model of schizophrenia can be formulated.

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References

1. Mueser KT, Bellack AS: Social skills and social functioning in schizophrenia, in Handbook of Social Functioning in Schizophrenia. Edited by Mueser KT, Tarrier N. Needham Heights, Mass, Allyn & Bacon, 1998, pp 79–98
2. Addington J, Addington D: Neurocognitive and social functioning in schizophrenia: a 2.5 year follow-up study. Schizophr Res 2000; 44:47–56
3. Davidson M, Reichenberg A, Rabinowitz J, Weiser M, Kaplan Z, Mark M: Behavioral and intellectual markers for schizophrenia in apparently healthy male adolescents. Am J Psychiatry 1999; 156:1328–1335
4. Hans SL, Auerbach JG, Asarnow JR, Styr B, Marcus J: Social adjustment of adolescents at risk for schizophrenia: the Jerusalem Infant Development Study. J Am Acad Child Adolesc Psychiatry 2000; 39:1406–1414
5. Perlick D, Stastny P, Mattis S, Teresi J: Contribution of family, cognitive, and clinical dimensions to long-term outcome in schizophrenia. Schizophr Res 1992; 6:257–265
6. Kern RS, Green MF, Marshall BD Jr, Wirshing WC, Wirshing D, McGurk SR, Marder SR, Mintz J: Risperidone versus haloperidol on secondary memory: can newer medications aid learning? Schizophr Bull 1999; 25:223–232
7. Green MF: What are the functional consequences of neurocognitive deficits in schizophrenia? Am J Psychiatry 1996; 153: 321–330
8. Green MF, Kern R, Braff DL, Mintz J: Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the right stuff? Schizophr Bull 2000; 26:119–136
9. Penn DL, Corrigan PW, Bentall RP, Racenstein JM, Newman L: Social cognition in schizophrenia. Psychol Bull 1997; 121:114–132
10. Penn DL, Corrigan PW, Racenstein JM: Cognitive factors and social adjustment in schizophrenia, in Handbook of Social Functioning in Schizophrenia. Edited by Mueser KT, Tarrier N. Needham Heights, Mass, Allyn & Bacon, 1998, pp 213–223
11. Fiske ST: Social cognition, in Advanced Social Psychology. Edited by Tesser A. New York, McGraw-Hill, 1995, pp 149–193
12. Adolphs R: The neurobiology of social cognition. Curr Opin Neurobiol 2001; 11:231–239
13. Brothers L: The social brain: a project for integrating primate behavior and neurophysiology in a new domain. Concepts in Neuroscience 1990; 1:27–51
14. Adolphs R: Social cognition and the human brain. Trends Cogn Sci 1999; 3:469–479
15. Anderson SW, Bechara A, Damasio H, Tranel D, Damasio AR: Impairment of social and moral behavior related to early damage in human prefrontal cortex. Nat Neurosci 1999; 2:1032–1037
16. Blair RJR, Cipolotti L: Impaired social response reversal: a case of "acquired sociopathy." Brain 2000; 123:1122–1141
17. Fine C, Lumsden J, Blair RJR: Dissociation between "theory of mind" and executive functions in a patient with early left amygdala damage. Brain 2001; 124:287–298
18. Kanwisher N: Domain specificity in face perception. Nat Neurosci 2000; 3:759–763
19. Jones W, Bellugi U, Lai Z, Chiles M, Reilly J, Lincoln A, Adolphs R: II: hypersociability in Williams syndrome. J Cogn Neurosci 2000; 12:30–46
20. Karmiloff-Smith A: Discussion in "Social Complexity and Social Intelligence" by Whiten A, in Symposium on the Nature of Intelligence. Edited by Bock GR, Goode JA, Webb K. Chichester, UK, John Wiley & Sons, 2000, p 199
21. Karmiloff-Smith A, Klima E, Bellugi U, Grant J, Baron-Cohen S: Is there a social module? language, face processing, and theory of mind in individuals with Williams syndrome. J Cogn Neurosci 1995; 7:196–208
22. Bellugi U, Lichtenberger L, Jones W, Lai Z, St George M: The neurocognitive profile of Williams syndrome: a complex pattern of strengths and weaknesses. J Cogn Neurosci 2000; 12(suppl):7–29
23. Tager-Flusberg H, Boshart J, Baron-Cohen S: Reading the windows to the soul: evidence of domain-specific sparing in Williams syndrome. J Cogn Neurosci 1998; 10:631–639
24. Heavey L, Phillips W, Baron-Cohen S, Rutter M: The awkward moments test: a naturalistic measure of social understanding in autism. J Autism Dev Disord 2000; 30:225–236
25. Klin A: Attributing social meaning to ambiguous visual stimuli in higher-functioning autism and Asperger syndrome: the social attribution task. J Child Psychol Psychiatry 2000; 41:831–846
26. Cosmides L, Tooby J: Beyond intuition and instinct blindness: toward an evolutionarily rigorous cognitive science. Cognition 1994; 50:41–77
27. Frith CD, Frith U: Interacting minds—a biological basis. Science 1999; 286:1692–1695

28. Corcoran R, Mercer G, Frith CD: Schizophrenia, symptomatology and social influence: investigating "theory of mind" in people with schizophrenia. Schizophr Res 1995; 17:5–13
29. Drury VM, Robinson EJ, Birchwood M: "Theory of mind" skills during an acute episode of psychosis and following recovery. Psychol Med 1998; 28:1101–1112
30. Frith CD, Corcoran R: Exploring "theory of mind" in people with schizophrenia. Psychol Med 1996; 26:521–530
31. Pilowsky T, Yirmiya N, Arbelle S, Mozes T: Theory of mind abilities in children with schizophrenia, children with autism, and normally developing children. Schizophr Res 2000; 42:145–155
32. Sarfati Y, Hardy-Bayle MC: How do people with schizophrenia explain the behaviour of others? a study of theory of mind and its relationship to thought and speech disorganization in schizophrenia. Psychol Med 1999; 29:613–620
33. Sarfati Y, Hardy-Bayle MC, Brunet E, Widloecher D: Investigating theory of mind in schizophrenia: influence of verbalization in disorganized and non-disorganized patients. Schizophr Res 1999; 37:183–190
34. Sarfati Y, Hardy-Bayle MC, Nadel J, Chevalier JF, Widloecher D: Attribution of mental states to others by schizophrenic patients. Cognitive Neuropsychiatry 1997; 2:1–17
35. Corcoran R: Theory of mind and schizophrenia, in Social Cognition in Schizophrenia. Edited by Corrigan PW, Penn DL. Washington, DC, American Psychological Association, 2001, pp 149–174
36. Doody GA, Gotz M, Johnstone EC, Frith CD, Cunningham-Owens DG: Theory of mind and psychoses. Psychol Med 1998; 28: 397–405
37. Mazza M, De Risio A, Surian L, Roncone R, Casacchia M: Selective impairments of theory of mind in people with schizophrenia. Schizophr Res 2001; 47:299–308
38. Pickup GJ, Frith CD: Theory of mind impairments in schizophrenia: symptomatology, severity, and specificity. Psychol Med 2001; 31:207–220
39. Edwards J, Jackson HJ, Pattison PE: Emotion recognition via facial expression and affective prosody in schizophrenia: a methodological review. Clin Psychol Rev 2002; 22:789–832
40. Hellewell JSE, Whittaker JF: Affect perception and social knowledge in schizophrenia, in Handbook of Social Functioning in Schizophrenia. Edited by Mueser KT, Tarrier N. Needham Heights, Mass, Allyn & Bacon, 1998, pp 197–212
41. Mandal MK, Pandey R, Prasad AB: Facial expressions of emotion and schizophrenia: a review. Schizophr Bull 1998; 24:399–412
42. Morrison RL, Bellack AS, Mueser KT: Deficits in facial-affect recognition and schizophrenia. Schizophr Bull 1988; 14:67–83
43. Edwards J, Pattison PE, Jackson HJ, Wales RJ: Facial affect and affective prosody recognition in first-episode schizophrenia. Schizophr Res 2001; 48:235–253
44. Evangeli M, Broks P: Face processing in schizophrenia: parallels with the effects of amygdala damage. Cognitive Neuropsychiatry 2000; 5:81–104
45. Addington J, Addington D: Facial affect recognition and information processing in schizophrenia and bipolar disorder. Schizophr Res 1998; 32:171–181
46. Gaebel W, Wolwer W: Facial expression and emotional face recognition in schizophrenia and depression. Eur Arch Psychiatry Clin Neurosci 1992; 242:46–52
47. Cutting J: Judgment of emotional expression in schizophrenia. Br J Psychiatry 1981; 139:1–6
48. Gessler S, Cutting J, Frith CD, Weinman J: Schizophrenic ability to judge facial emotion: a controlled study. Br J Clin Psychol 1989; 28:19–29
49. Davis PJ, Gibson MG: Recognition of posed and genuine facial expressions of emotion in paranoid and nonparanoid schizophrenia. J Abnorm Psychol 2000; 109:445–450
50. Kline J, Smith JE, Ellis HC: Paranoid and nonparanoid schizophrenic processing of facially displayed affect. J Psychiatr Res 1992; 26:169–182
51. Lewis SF, Garver DL: Treatment and diagnostic subtype in facial affect recognition in schizophrenia. J Psychiatr Res 1995; 29:5–11
52. Mandal MK, Rai A: Responses to facial emotion and psychopathology. Psychiatry Res 1987; 20:317–323
53. Bellack AS, Blanchard JJ, Mueser KT: Cue availability and affect perception in schizophrenia. Schizophr Bull 1996; 22:535–544
54. Kerr SL, Neale JM: Emotion perception in schizophrenia: specific deficit or further evidence of generalized poor performance? J Abnorm Psychol 1993; 102:312–318
55. Mueser KT, Doonan R, Penn DL, Blanchard JJ, Bellack AS, Nishith P, DeLeon J: Emotion recognition and social competence in chronic schizophrenia. J Abnorm Psychol 1996; 105: 271–275
56. Salem JE, Kring AM, Kerr SL: More evidence for generalized poor performance in facial emotion performance in schizophrenia. J Abnorm Psychol 1996; 105:480–483
57. Heimberg C, Gur RE, Erwin RJ, Shatasel DL, Gur RC: Facial emotion discrimination, III: behavioral findings in schizophrenia. Psychiatry Res 1992; 43:253–265
58. Penn DL, Combs D, Ritchie M, Francis J, Cassisi J, Morris S, Townsend M: Emotion recognition in schizophrenia: further investigation of specific versus generalized performance deficit models. J Abnorm Psychol 2000; 109:512–516
59. Archer J, Hay DC, Young AW: Movement, face processing, and schizophrenia: evidence of a differential deficit in expression analysis. Br J Clin Psychol 1994; 33:517–528
60. Bell M, Bryson G, Lysaker P: Positive and negative affect recognition in schizophrenia: a comparison with substance abuse and normal control subjects. Psychiatry Res 1997; 73:73–82
61. Corrigan PW, Addis IB: The effect of cognitive complexity on a social sequencing task in schizophrenia. Schizophr Res 1995; 16:137–144
62. Corrigan PW, Davies-Farmer RM, Stolley MR: Social cue recognition in schizophrenia under variable levels of arousal. Cognit Ther Res 1990; 14:353–361
63. Leonhard C, Corrigan PW: Social perception in schizophrenia, in Social Cognition in Schizophrenia. Edited by Corrigan PW, Penn DL. Washington, DC, American Psychological Association, 2001, pp 73–95
64. Bentall RP: The illusion of reality: a review and integration of psychological research on hallucinations. Psychol Bull 1990; 107:82–95
65. Morrison AP, Haddock G: Cognitive factors in source monitoring and auditory hallucinations. Psychol Med 1997; 27:669–679
66. Bentall RP: Social cognition and delusional beliefs, in Social Cognition in Schizophrenia. Edited by Corrigan PW, Penn DL. Washington, DC, American Psychological Association, 2001, pp 123–148
67. Bentall RP, Corcoran R, Howard R, Blackwood N, Kinderman P: Persecutory delusions: a review and theoretical integration. Clin Psychol Rev 2001; 21:1143–1192
68. Kristev H, Jackson H, Maude D: An investigation of attributional style in first-episode psychosis. Br J Clin Psychol 1999; 88:181–194
69. Martin JA, Penn DL: Attributional style in schizophrenia: an investigation in outpatients with and without persecutory delusions. Schizophr Bull 2002; 28:131–141

70. Garety PA, Freeman D: Cognitive approaches to delusions: a critical review of theories and evidence. Br J Clin Psychol 1999; 38:113–154
71. Kinderman P, Bentall RP: Causal attributions in paranoia and depression: internal, personal, and situational attributions for negative events. J Abnorm Psychol 1997; 106:341–345
72. Penn DL, Combs D, Mohamed S: Social cognition and social functioning in schizophrenia, in Social Cognition in Schizophrenia. Edited by Corrigan PW, Penn DL. Washington, DC, American Psychological Association, 2001, pp 97–121
73. Penn DL, Spaulding W, Reed D, Sullivan M: The relationship of social cognition to ward behavior in chronic schizophrenia. Schizophr Res 1996; 20:327–335
74. Ihnen GH, Penn DL, Corrigan PW, Martin J: Social perception and social skill in schizophrenia. Psychiatry Res 1998; 80:275–286
75. Penn DL, Corrigan PW, Martin J, Ihnen G, Racenstein JM, Nelson D, Cassisi J, Hope DA: Social cognition and social skills in schizophrenia: the role of self-monitoring. J Nerv Ment Dis 1999; 187: 188–190
76. Appelo MT, Woonings FMJ, van Nieuwenhuizen CJ, Emmelkamp PMG, Slooff CJ, Louwerens JW: Specific skills and social competence in schizophrenia. Acta Psychiatr Scand 1992; 85:419–422
77. Penn DL, Ritchie M, Francis J, Combs D, Martin J: Social perception in schizophrenia: the role of context. Psychiatry Res 2002; 109:149–159
78. Bellack AS, Mueser KT, Wade J, Sayers S, Morrison RL: The ability of schizophrenics to perceive and cope with negative affect. Br J Psychiatry 1992; 160:473–480
79. Corrigan PW, Toomey R: Interpersonal problem solving and information processing in schizophrenia. Schizophr Bull 1995; 21:395–403
80. Toomey R, Wallace CJ, Corrigan PW, Schuldberg D, Green MF: Social processing correlates of nonverbal social perception in schizophrenia. Psychiatry 1997; 60:292–300
81. Hooker C, Roese NJ, Park S: Impoverished counterfactual thinking is associated with schizophrenia. Psychiatry 2000; 63:326–335
82. Adolphs R: Recognizing emotion from facial expressions: psychological and neurological mechanisms. Behavioral and Cognitive Neuroscience Rev 2002; 1:21–62
83. Baron-Cohen S, Ring H, Moriarty J, Schmitz B, Costa D, Ell P: Recognition of mental state terms: clinical finding in children with autism and a functional neuroimaging study of normal adults. Br J Psychiatry 1994; 165:640–649
84. Stone VE, Baron-Cohen S, Knight RT: Frontal lobe contributions to theory of mind. J Cogn Neurosci 1998; 10:640–656
85. Allison T, Puce A, McCarthy G: Social perception from visual cues: role of the STS region. Trends Cogn Sci 2000; 4:267–278
86. Frith U: Mind blindness and the brain in autism. Neuron 2001; 32:969–979
87. Fletcher PC, Happe F, Frith U, Baker SC, Dolan RJ, Frackowiak RSJ: Other minds in the brain: a functional imaging study of "theory of mind" in story comprehension. Cognition 1995; 57: 109–128
88. Goel V, Grafman J, Sadato N, Hallett M: Modeling other minds. Neuroreport 1995; 6:1741–1746
89. Stuss DT, Gallup GG Jr, Alexander MP: The frontal lobes are necessary for "theory of mind." Brain 2001; 124:279–286
90. McCabe K, Houser D, Ryan L, Smith V, Trouard T: A functional imaging study of cooperation in two-person reciprocal exchange. Proc Natl Acad Sci USA 2001; 98:11832–11835
91. Vogeley K, Bussfeld P, Newen A, Herrmann S, Happe F, Falkai P, Maier W, Shah NJ, Fink GR, Zilles K: Mind reading: neural mechanisms of theory of mind and self-perspective. Neuroimage 2001; 14:170–181
92. Gallagher HL, Happe F, Brunswick N, Fletcher PC, Frith U, Frith CD: Reading the mind in cartoons and stories: an fMRI study of "theory of mind" in verbal and nonverbal tasks. Neuropsychologia 2000; 38:11–21
93. Brunet E, Sarfati Y, Hardy-Bayle M, Decety J: A PET investigation of the attribution of intentions with a nonverbal task. Neuroimage 2000; 11:157–166
94. Castelli F, Happe F, Frith U, Frith C: Movement and mind: a functional imaging study of perception and interpretation of complex intentional movement patterns. Neuroimage 2000; 12:314–325
95. Happe F, Ehlers S, Fletcher P, Frith U, Johansson M, Gillberg C: "Theory of mind" in the brain: evidence from a PET scan study of Asperger syndrome. Neuroreport 1996; 8:197–201
96. Arnold SE, Trojanowski JQ: Recent advances in defining the neuropathology of schizophrenia. Acta Neuropathol (Berl) 1996; 92:217–231
97. Wright IC, Rabe-Hesketh S, Woodruff PWR, David AS, Murray RM, Bullmore ET: Meta-analysis of regional brain volumes in schizophrenia. Am J Psychiatry 2000; 157:16–25
98. Convit A, Wolf OT, de Leon MJ, Patalinjug M, Kandil E, Caraos C, Scherer A, Saint Louis LA, Cancro R: Volumetric analysis of the pre-frontal regions: findings in aging and schizophrenia. Psychiatry Res 2001; 107:61–73
99. Crespo-Facorro B, Kim J, Andreasen NC, O'Leary DS, Magnotta V: Regional frontal abnormalities in schizophrenia: a quantitative gray matter volume and cortical surface size study. Biol Psychiatry 2000; 48:110–119
100. Gur RE, Cowell PE, Latshaw A, Turetsky BI, Grossman RI, Arnold SE, Bilker WB, Gur RC: Reduced dorsal and orbital prefrontal gray matter volumes in schizophrenia. Arch Gen Psychiatry 2000; 57:761–768
101. Marsh L, Lim KO, Hoff AL, Harris D, Beal M, Minn K: Severity of schizophrenia and magnetic resonance imaging abnormalities: a comparison of state and veterans hospital patients. Biol Psychiatry 1999; 45:49–61
102. Paillere-Martinot ML, Caclin A, Artiges E, Poline JB, Joliot M, Mallet L, Recasens C, Attar-Levy D, Martinot JL: Cerebral gray and white matter reduction and clinical correlates in patients with early-onset schizophrenia. Schizophr Res 2001; 50:19–26
103. Staal WG, Hulshoff Pol HE, Schnack HG, Hoogendoorn MLC, Jellema K, Kahn RS: Structural brain abnormalities in patients with schizophrenia and their healthy siblings. Am J Psychiatry 2000; 157:416–421
104. Sanfilipo M, Lafargue T, Rusinek H, Arena L, Loneragan C, Lautin A, Feiner D, Rotrosen J, Wolkin A: Volumetric measure of the frontal and temporal lobe regions in schizophrenia: relationship to negative symptoms. Arch Gen Psychiatry 2000; 57:471–480
105. Rajkowska G, Selemon LD, Goldman-Rakic PS: Neuronal and glial somal size in the prefrontal cortex: a postmortem morphometric study of schizophrenia and Huntington disease. Arch Gen Psychiatry 1998; 55:215–224
106. Malaspina D, Storer S, Furman V, Esser P, Printz D, Berman A, Lignelli A, Gorman J, Van Heertum R: SPECT study of visual fixation in schizophrenia and comparison subjects. Biol Psychiatry 1999; 46:89–93
107. Kawasaki Y, Maeda Y, Suzuki M, Urata K, Higashima M, Kiba K, Yamaguchi N, Matsuda H, Hisada K: SPECT analysis of regional cerebral blood flow changes in patients with schizophrenia during the Wisconsin Card Sorting Test. Schizophr Res 1993; 10:109–116
108. Volz HP, Nenadic I, Gaser C, Rammsayer T, Haeger F, Sauer H: Time estimation in schizophrenia: an fMRI study at adjusted levels of difficulty. Neuroreport 2001; 12:313–316
109. Russell TA, Rubia K, Bullmore ET, Soni W, Suckling J, Brammer MJ, Simmons A, Williams SCR, Sharma T: Exploring the social

brain in schizophrenia: left prefrontal underactivation during mental state attribution. Am J Psychiatry 2000; 157:2040–2042
110. Chao LL, Martin A, Haxby JV: Are face-responsive regions selective only for faces? Neuroreport 1999; 10:2945–2950
111. Puce A, Allison T, Asgari M, Gore JC, McCarthy G: Differential sensitivity of human visual cortex to faces, letterstrings, and textures: a functional magnetic resonance imaging study. J Neurosci 1996; 16:5205–5215
112. Haxby JV, Hoffmann EA, Gobbini MI: The distributed human neural system for face perception. Trends in Cognitive Sciences 2000; 4:223–232
113. Blackwood NJ, Howard RJ, Bentall RP, Murray RM: Cognitive neuropsychiatric models of persecutory delusions. Am J Psychiatry 2001; 158:527–539
114. Adolphs R, Tranel D, Hamann S, Young AW, Calder AJ, Phelps EA: Recognition of facial emotion in nine individuals with bilateral amygdala damage. Neuropsychologia 1999; 37:1111–1117
115. Calder AJ, Young AW, Rowland D, Perrett DI, Hodges JR, Etcoff NL: Facial emotion recognition after bilateral amygdala damage: differentially severe impairment of fear. Cognitive Neuropsychology 1996; 13:699–745
116. Young AW, Aggleton JP, Hellawell DJ, Johnson M, Broks P, Hanley JR: Face processing impairments after amygdalotomy. Brain 1995; 118:15–24
117. Adolphs R, Tranel D, Damasio AR: The human amygdala in social judgment. Nature 1998; 393:470–474
118. Morris JS, Frith CD, Perrett DI, Rowland D, Young AW, Calder AJ: A differential neural response in the human amygdala to fearful and happy facial expressions. Nature 1996; 383:812–815
119. Whalen P, Rauch S, Etcoff N, McInerney S, Lee M, Jenike M: Masked presentations of emotional facial expressions modulate amygdala activity without explicit knowledge. J Neurosci 1998; 18:411–418
120. Phillips ML, Young AW, Senior C, Brammer M, Andrews C, Calder AJ: A specific neural substrate for perceiving facial expressions of disgust. Nature 1997; 389:495–498
121. Winston JS, Strange BA, O'Doherty J, Dolan RJ: Automatic and intentional responses during evaluation of trustworthiness of faces. Nat Neurosci 2002; 5:277–283
122. McDonald B, Highley JR, Walker MA, Herron BM, Cooper SJ, Esiri MM, Crow TJ: Anomalous asymmetry of fusiform and parahippocampal gyrus gray matter in schizophrenia: a postmortem study. Am J Psychiatry 2000; 157:40–47
123. Buchanan RW, Breier A, Kirkpatrick B, Elkashef A, Munson RC, Gellad F, Carpenter WT Jr: Structural abnormalities in deficit and nondeficit schizophrenia. Am J Psychiatry 1993; 150:59–65
124. Pearlson GD, Garta PE, Powers RE, Menon RR, Richards SS, Aylward EH, Federman EB, Chase GA, Petty RG, Tien AY: Medial and superior temporal gyral volumes and cerebral asymmetry in schizophrenia versus bipolar disorder. Biol Psychiatry 1997; 41:1–14
125. Nelson MD, Saykin AJ, Flashman LA, Riordan HJ: Hippocampal volume reduction in schizophrenia as assessed by magnetic resonance imaging. Arch Gen Psychiatry 1998; 55:433–440
126. Schneider F, Weiss U, Kessler C, Salloum JB, Posse S, Grodd W, Mueller-Gaertner HW: Differential amygdala activation in schizophrenia during sadness. Schizophr Res 1998; 34:133–142
127. Phillips ML, Williams L, Senior C, Bullmore ET, Brammer MJ, Andrew C, Williams SC, David AS: A differential neural response to threatening and non-threatening negative facial expressions in paranoid and non-paranoid schizophrenics. Psychiatry Res Neuroimaging 1999; 92:11–31
128. Bechara A, Damasio H, Damasio AR, Lee GP: Different contributions of the human amygdala and ventromedial prefrontal cortex to decision-making. J Neurosci 1999; 19:5473–5481
129. Bechara A, Dolan S, Denburg N, Hindes A, Anderson SW, Nathan PE: Decision-making deficits, linked to a dysfunctional ventromedial prefrontal cortex, revealed in alcohol and stimulant abusers. Neuropsychologia 2001; 39:376–389
130. Penn D, Ritchie M, Francis J, Combs D, Martin J: Social perception in schizophrenia: the role of context. Psychiatry Res 2002; 109:149–159
131. Corrigan PW, Addis IB: The effect of cognitive complexity on a social sequencing task in schizophrenia. Schizophr Res 1995; 16:137–144
132. Amminger GP, Pape S, Rock D, Roberts SA, Ott SL, Squires-Wheeler E, Kestenbaum C, Erlenmeyer-Kimling L: Relationship between childhood behavioral disturbance and later schizophrenia in the New York High-Risk Project. Am J Psychiatry 1999; 156:525–530
133. Baum K, Walker E: The relation between childhood behavior problems and clinical symptoms in adult-onset schizophrenia. Schizophr Res 1995; 16:111–120
134. Cannon M, Walsh E, Hollins C, Kargin M, Taylor E, Murray RM, Jones PB: Predictors of later schizophrenia and other affective psychosis among attendees at a child psychiatry department. Br J Psychiatry 2001; 178:420–426
135. Done DJ, Crow TJ, Johnstone EC, Sacker A: Childhood antecedents of schizophrenia and affective illness: social adjustment at ages 7 and 11. Br Med J 1994; 309:699–703
136. Litter J, Walker E: Interpersonal behavior of preschizophrenic children: a study of home movies. Child Psychiatry Hum Dev 1993; 23:283–295
137. Mirsky AF, Kugelmass S, Ingraham LJ, Frenkel E, Nathan M: Overview and summary: twenty-five-year followup of high-risk children. Schizophr Bull 1995; 21:227–239
138. Rossi A, Pollice R, Daneluzzo E, Marinangeli MG, Stratta P: Behavioral neurodevelopmental abnormalities and schizophrenic disorder: a retrospective evaluation with the Child Behavior Checklist (CBCL). Schizophr Res 2000; 44:121–128
139. Olin SC, Mednick SA: Risk factors of psychosis: identifying vulnerable populations. Schizophr Bull 1996; 22:223–240
140. Olin SC, Mednick SA, Cannon T, Jacobsen B, Parnas J, Schulsinger F, Schulsinger H: School teacher ratings predictive of psychiatric outcome 25 years later. Br J Psychiatry Suppl 1998; 172:7–13
141. Fenkel E, Kugelmass S, Nathan M, Ingraham LJ: Locus of control and mental health in adolescence and adulthood. Schizophr Bull 1995; 21:219–226
142. Cornblatt B, Obuchowski M, Roberts S, Pollack S, Erlenmeyer-Kimling L: Cognitive and behavioral precursors of schizophrenia. Dev Psychopathol 1999; 11:487–508
143. Mueser KT, Bond GR: Psychosocial treatment approaches for schizophrenia. Curr Opin Psychiatry 2000; 13:27–35
144. Combs DR, Penn DL: The role of subclinical paranoia on social perception and behavior. Schizophr Res (in press)