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The study of social cognition with neuroimaging methods as a means to explore future directions of deficit evaluation in schizophrenia?

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ABSTRACT

This article discusses the important advances in a recent field of science dealing with the brain processes implicated in understanding social situations and interacting with others. Many behavioral studies on schizophrenia have shown the impairment of these processes and their preferential relation with disorganization and negative syndromes. Brain imaging is a powerful method to identify brain systems participating in these processes in healthy subjects and will be used increasingly to study mental disorders such as schizophrenia. A few preliminary studies have opened this field of research and allowed for the drawing of some limited conclusions. We emphasize the importance of developing an integrated neurocognitive framework to account for the multifaceted nature of social cognition deficits in schizophrenia. Inspired by contemporary models of empathy and social cognition that identify different components such as shared representation, mentalizing, self/other distinction, we show how schizophrenia affects these components at the behavioral and functional levels. We also outline the interest of this model to understand putative abnormalities of contextual integration within the area of mentalization. Finally, we discuss how specialized measures of brain functions during the performance of these precisely defined mental processes might be used as outcome predictors.

1. Introduction

Schizophrenia is associated with a severe social handicap resulting in a drastic reduction of autonomy and of professional and personal achievements, and in the disruption of family and peer relations. Contrary to widespread intuition, several authors showed that these central aspects of prognosis are only weakly predicted by symptoms (Rosen and Garety, 2005; Wykes and Reeder, 2005; Brüne et al., 2007). The limited performance of clinical evaluations to discriminate the severity of the illness or to define therapeutic strategies has led to the proposal of new evaluation techniques and tools, many of them inspired by neuropsychological assessment. This was, for instance, the rationale for the initiative Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) of the National Institute of Mental Health (NIMH) that offered, from a consensus of experts, a neuropsychological battery to promote cognitive disorders as a target of pharmaceutical treatment (Marder et al., 2004). In addition, this proposal recognized explicitly the role of social cognition, among other domains such as attention, executive function, and working memory, to determine a patient's status beyond clinical evaluations. Given their objectives oriented at pharmaceutical research, MATRICS experts did not provide an integrated view of social cognition based on recent research in this domain. In the present article, we will take into account the emergence of a new field of research dealing with the neurocognitive processes involved in social behavior that recently offered both theoretical and experimental insights into the abnormal processes of schizophrenia. Importantly, social cognition appears promising to offer a convergent point of scattered research in several domains such as theory of mind, emotion perception, metacognition, cognitive remediation, and functional outcome evaluation.

This article provides an overview of research in the field, taking selectively into account results from behavioral research (section 2) to neuroimaging studies (sections 4, 5, and 6). We stress the relevance of models, coming from social and affective neurosciences, and propose a cognitive framework inspired by current models (section 3). In sections 7, 8, and 9, we outline three perspectives of research that would merit investigations using functional neuroimaging. We conclude by emphasizing the importance of this literature in assessing the illness course and outcome (section 10).

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2. Insights from behavioral and clinical studies

As will be discussed in the following, social cognition does not constitute a unitary construct (Farrow, 2007) and is not even a function per se. Often classified as a hybrid between an emotional and a cognitive phenomenon, social cognition encompasses many aspects as follows: gesture social perception, eye-gaze detection, emotion perception, empathy, agency and self/other distinction, mentalizing (also known as theory of mind), recognition of intentional causality or intentionality, etc. Most of the time, these aspects have been assessed separately in schizophrenia, revealing abnormal performances. The ability for processing emotional mental states has, on the one hand, most often been assessed through emotion recognition tasks, although a few studies have also targeted empathy. The performance for processing of more cognitive mental states such as beliefs or intentions has on the other hand been studied mainly through mentalizing paradigms.

To begin with, the processing of emotional states, recognition and categorization, measured either through basic facial emotion tasks (emotion identification or recognition) or prosody recognition, demonstrates consistent abnormalities in people with schizophrenia, although the relations of these cognitive functions with symptoms remain debate (see meta-analyses and reviews in Hoekert et al., 2007; Kohler et al., 2010). A more recent field of research also highlights abnormal empathic judgments, encompassing emotions that are more complex or dispositions to others' feelings (Shamay-Tsoory et al., 2007a, 2007b, 2007c; Bora et al., 2008). First, Haker and Rossler (2009) recently brought evidence for impairments in empathic resonance, i.e. "the phenomenon of one person unconsciously mirroring the motor action as basis of emotional expressions of another person," in schizophrenia. In this study, videos of laughing and yawning led to reduced contagious behaviors in patients compared to healthy participants. Second, a recent study by Derntl et al. (2009) demonstrated that patients with schizophrenia presented deficits in several aspects of empathy such as emotion recognition, sharing emotional states and emotional perspective taking. Although, to the best of our knowledge, there is as yet no report on large cohorts of patients, a meta-analysis showed that patients with schizophrenia self-report (Davis' Interpersonal Reactivity Index) a lower inclination to take the perspective of others but higher levels of personal distress than healthy controls (Achim et al., 2011). In addition, the perspective taking impairment seems to increase during the course of the illness (Montag et al., 2007) and studies with first episode patients generally showed smaller effect sizes (Achim et al., 2011). The relationship between these empathic abilities and clinical symptoms remains, however, unclear.

On the cognitive or "less affective" side and inspired by previous studies in autistic populations, the skills of inferring others' mental states, i.e. mentalizing, is amongst the most investigated aspects in schizophrenia. Several dozens of studies are now available and allowed meta-analytic approaches revealing that mentalizing deficits are of comparable or even higher magnitude (Sprong et al., 2007; Bora et al., 2009) than the deficits observed on standard nonsocial neuropsychological measures (Heinrichs and Zakzanis, 1998). In line with this idea, a recent study by Bertrand et al. (2007) showed that social cognitive measures have the greatest effect sizes among other neuropsychological assessments in patients with a first episode psychosis. From the many studies available, it follows that several categories of tests exhibit large effect sizes, regardless of the type of mental states being inferred (intentions, false beliefs, etc.) or of the modality of presentation (verbal, nonverbal, both) (Sprong et al., 2007).

Knowledge of the association between mentalizing deficits and clinical symptoms has been enhanced by accumulated empirical evidence. One of the aforementioned meta-analyses has emphasized the importance of social deficits in negative as well as in disorganized patients (Sprong et al., 2007). Recent findings obtained by some of us, with a large sample of patients assessed with a video-based intention attribution task (Bourdet et al., 2008; Bazin et al., 2009), demonstrate the preferential relations of mentalizing deficits with some Positive and Negative Syndrome Scale (PANSS) items. Among these items, one can find affective blunting, social withdrawal, difficulty of abstraction, conceptual disorganization, and attention deficits (Pearson's correlation coefficients ranging from 0.20 to 0.34, $n=217$ medicated patients, $p<0.05$). Let us note again that age (as well as duration of illness) constitutes an aggravating factor, albeit one that is nonspecific. Interestingly, no item belonging to the positive syndrome exhibited significant correlation with impaired attribution of intentions in our study. In addition, significant correlations were found with communication disorders (Pearson's correlation coefficients with SCD global score of 0.41, $n=215$) evaluated during semi-structured interviews guided by pragmatic conversational constraints and requiring theory of mind judgments (see description of the Communication Disorder Scale, SCD, in Olivier et al., 1997; Bazin et al., 2005). Similar associations between impaired attribution capabilities and the disorganization syndrome (but not positive symptoms) were confirmed by Abdel-Hamid et al. (2009) with a comic-strip sequencing task in which subjects had to rearrange pictures depicting complex social situations. On the other hand, a recent study showed impairments in understanding intentions of protagonists of short videos in schizophrenia-spectrum patients having persecutory delusions in comparison with patients not suffering from such a symptom (Mehl et al., 2010a, 2010b). To the best of our knowledge, neuroimaging research has not produced significant advances in determining the relations between symptoms and social cognitive deficits. One could argue that future research based on measures of brain correlates of social cognition should test the correlations with disorganization, negative and positive syndromes.

The association between social and more traditional measures of cognition has also been the subject of a number of investigations. In the literature with healthy individuals, an ongoing debate focuses on the modular versus separable nature of social cognition (discussion in Beer and Ochsner, 2006). A similar issue was raised in schizophrenia research introducing an evolutionary and developmental perspective (Brüne and Brüne-Cohrs, 2006). Deficits of social cognition seem to remain significant even after controlling for deficits in other cognitive domains. Brüne (2005) concluded an overview of the literature with this statement: "While attention deficits, executive dysfunction, and lower intelligence scores negatively influence performance on ToM tasks, differences between schizophrenia subjects and healthy control persons in task performance remain significant, even when general cognitive deficits and measures of executive functioning are controlled for" (p. 25). This convincing interpretation of replicated behavioral observations is tricky, however, as causal relations between impairments in social and nonsocial skills are hard to disentangle. Indeed, compensation of deficits in social cognition by nonsocial mechanisms may explain partial correlations between these domains. In short, it seems very difficult to tease apart the contribution of different domains by measuring only behavioral performances. Brain functional cartography, as a means to measure the respective contributions of these processes to which behavioral measures are blind, appears promising.

3. The needs for an integrative model of social cognition

Several conceptual frameworks have been proposed to guide experimentations on social cognition in schizophrenia research. Some psychopathological models such as the one described by Couture et al. (2010) aimed to explain the disorder in order to predict functional outcome. According to these authors, interpretations of social or emotional cues depend on the patient's attributional style (for instance, a personalizing bias), which in turn is influenced by theory of mind inferences. Although this model has undeniable merits in